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The Glycosuria of Hyperthyroidism and Its Clinical Significance*

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GLYCOSURIA is not infrequently met with in cases of hyperthyroidism. As in pregnancy, however, if urinalyses are made at frequent intervals rather than on special occasions, its incidence is found to be much greater than recorded in standard text books. It is somewhat related to the basal metabolic rate; the higher the rate, the greater is the incidence. This probably accounts for the fact that glycosuria is met with more frequently in exophthalmic goitre than in so-called "secondary" hyperthyroidism associated with adenomata. The relationship between basal metabolism and glycosuria will, again, be referred to, as the above statement requires modification. The literature on this subject is quite extensive. However, as it is readily available, in review form[1,2,3,4], and for purposes of brevity, no summary of it will be given here, with the exception of reference to relevant facts.

When glycosuria is found, the determination of the cause is more than of academic interest, as it influences treatment. In hyperthyroidism, when the rate of metabolism is markedly increased, there may be marked destruction of vital body tissue, namely, protein, as shown by the excretion of urinary nitrogen. (Urinary nitrogen is a reliable index of protein metabolism). With destruction of large quantities of protein a vicious circle may result, since protein utilization, per se, may, because of its specific dynamic action, be responsible for increased rate of metabolism. Thus, increased metabolism due to hyperthyroidism leads to increased protein destruction and increased protein destruction further increases metabolism. Much of body protein may be conserved in such cases and rate of metabolism thereby lowered by administration of diets of high carbohydrate content, because of their protein sparing effects. On the other hand, if the glycosuria is due to diabetes, the use of such diets, without the use of insulin, would be harmful.

From the clinical picture alone, it is impossible, in the great majority of cases, to determine the cause of the glycosuria, as the signs and symptoms of hyperthyroidism and diabetes may be quite similar. As a matter of fact, the more marked the hyperthyroidism, the more do the signs and symptoms of this disease simulate those of diabetes. For example, in both cases, there may

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be marked weakness, loss of weight, polyuria and thirst. When the hyperthyroidism is more marked and the metabolic rate is very high, in addition to the above mentioned signs and symptoms, one may find flushed skin, increased pulmonary ventilation, a rapid and bounding pulse and, the urine, in addition to containing sugar, may, also, contain acetone and diacetic acid. In other words, the signs and symptoms of severe hyperthyroidism may be almost identical with those of severe diabetes with acidosis. As a matter of fact, Wilder[2], who has had a very wide experience with both diseases, suggests the use of iodine in severe cases of diabetes as a therapeutic test to rule out thyroid disease. In diabetes, uncomplicated by hyperthyroidism, iodine is without observable effects.

There is additional reason for determining the true cause of the glycosuria. If it is due to hyperthyroidism only, with the disappearance of the latter, following thyroidectomy or other measures, the glycosuria also disappears. Should the glycosuria have been attributed to diabetes, in such a case, it is obvious that one would regard the diabetes as having been cured. As a matter of fact, the literature is not without such "cures." Authentic cases of cured diabetes, if there are any at all, are extremely rare.

Judging from the literature, there is no uniform procedure for differentiating the glycosuria of hyperthyroidism from that of diabetes. One of the most common methods made use of is the study of fasting and post-prandial blood sugars. In the latest edition of his "Treatment of Diabetes" Joslin[4] states that "Ordinarily a patient is said to have diabetes who has certain characteristic symptoms, glycosuria varying with the diet and hyperglycemia above 0.13 per cent before or above 0.16 per cent after a meal. For the purposes of differentiating between the glycosuria of diabetes and of hyperthyroidism and in order to avoid premature diabetic cures, we have raised the standard for a diagnosis in hyperthyroidism to a blood sugar of 0.15 per cent fasting and 0.20 per cent or more after meals in addition to glycosuria." Marsh[5] makes use of simultaneously determined respiratory metabolism and blood sugar time curves. John[3] uses blood sugar time curves only. We, in addition to the method described by Marsh, make use of another procedure, the details of which will presently be discussed. It is based upon Allen's Paradoxical Law, namely, that, in the absence of true diabetes, there is no limit of tolerance for carbohydrates—the more given the more is utilized. This procedure is of special value because of its applicability in general practice and will be described later in detail.

The belief that the glycosuria of hyperthyroidism differs fundamentally from that of true diabetes is so general, one would hardly be justified in renewing the discussion, were it not for the new views recently advanced by John[3]. This author is apparently quite convinced that the hyperglycemia and glycosuria noted in this disease are the result of defective oxidation of carbohydrates and this defective oxidation is attributed to defective insulin production. In other words, it is implied that we are dealing essen-

tially with a diabetic condition. Because of this view, John warns that it is a very serious matter to disregard such glycosuria. If this view is correct, the present practice of giving such patients high carbohydrate diets without insulin is obviously not logical. It is, therefore, important to reconsider this subject.

The practical value of explanations of clinical phenomena may be said to be directly proportionate to their support by clinical experience and experimental facts. In support of his views, John quotes the extensive literature which includes theoretical, clinical and experimental data. It is, however, of interest here to note that from the same data made use of by John, it is possible to draw diametrically opposite conclusions.

Anatomical Considerations

As anatomical evidence to support his views, John quotes the findings of Holst[6], Rohdenberg[7], Garrod[8], Marinesco and Parhon[9], Falta[10] and Lorand[11]. From these, he concludes that there is a casual relationship between Graves' disease and diabetes. To quote verbatim, "There is reason to believe that in Graves' disease the well known anomalies in sugar metabolism are induced by gross anatomical changes in the pancreas . . . etc." With respect to this, two observations may be made. Firstly, the fact that histological changes in the pancreas may be found in Graves' disease is not necessarily proof that the association is causal; it may be accidental. Strongly suggestive that it is accidental are the low incidence of diabetes amongst individuals suffering from Graves' disease and the low incidence of a history of Graves' disease amongst diabetics. John, in an excellent review, tabulates the cases of combined diabetes and hyperthyroidism, according to the literature, from 1867 to 1927. In all there were 137 cases. In the latest edition of his "Treatment of Diabetes," Joslin reports 75 such cases amongst 4917 diabetics. Joslin, also, quotes Wilder who, amongst 1249 cases of diabetes found 1.1 per cent "primary" hyperthyroidism and 1.8 per cent of "secondary" hyperthyroidism. According to these percentages, there were approximately 36 cases of combined hyperthyroidism and diabetes amongst 1249 diabetics. Amongst the 3000 diabetics, in our clinic, there are 24 cases.

Opposed to the histological findings referred to are the negative findings of others. It may here be observed that the cases particularly of value in such investigation are, obviously, not those of diabetes and hyperthyroidism combined but of hyperthyroidism alone. Our pathologist, Dr. L. J. Rhea, tells me that in a careful study of ten fatal cases of Graves' disease, nothing significant could be detected in the pancreatic tissues.* These findings are identical with those of Joslin[4] who quotes Shields Warren and concludes that "The whole question deserves reinvestigation." Apropos of positive findings, Shields Warren, who has had an exceptional experience with the pathology of diabetes, very aptly points out in his excellent monograph on the subject[12] that "It is important to keep

*A-23-70, A-25-143, A-25-263, A-26-42, A-26-27, A-26-100, A-27-176, A-28-25, A-28-233, A-29-169.

in mind the great difficulties facing any estimate of the number of islands present in the human pancreas and the wide range in number of islands known to be present normally." In a study of five autopsied cases of diabetes associated with hyperthyroidism, the same author, found the islands of Langerhans were negative in all except one case and concludes "There is absolutely no characteristic picture."

Assuming, however, that positive findings are frequent and causal, it does not necessarily follow that diabetes and hyperthyroidism are related. It has been repeatedly emphasized that anatomical and functional integrity are not necessarily synonymous terms. The most one can conclude from the anatomical data is that there appears to be a functional relationship between the thyroid and the pancreas. For this, however, no anatomical evidence is necessary. For example, physiologists demonstrated sometime ago that, in the regulation of the blood sugar, the pancreas, thyroid and other organs of internal secretion (adrenal and pituitary bodies, etc.) are intimately concerned. Thus, thyroidectomy enhances the action of insulin; rabbits have been found to be 3 to 9 times as sensitive to insulin as before operation. However, after thyroidectomy, rabbits are also less sensitive to adrenalin. Also, following removal of the adrenal bodies, the characteristic hyperglycemic response to stimulation of the Claude Bernard centre is not obtained. These findings led to the suggestion that the adrenal bodies are the active agents in the production of hyperglycemia. Adrenalin is secreted into the general circulation, reaches the liver by the hepatic artery as well as the portal vein and also enters the muscles and mobilizes the sugar there. The adrenal bodies will, again, be referred to in dealing with signs and symptoms. Other and more recent experiments of Burns and Marks[13] and Bodansky[14] and similarly suggestive are discussed by Joslin[4].

Clinical Considerations

A clinical fact which remains to be explained is that in many cases, according to the literature, the history of diabetes followed, rather than preceded, the history of hyperthyroidism. It may, however, here be observed that diabetes following hyperthyroidism and diabetes caused by hyperthyroidism are, obviously, not synonymous terms. As a matter of fact, a careful study by the writer of the cases reported failed to reveal, according to our present standard methods of studies, an authentic case of diabetes resulting from hyperthyroidism. In our hospital, with a fairly large Goitre Clinic, Dr. E. M. Eberts, who is in charge, tells me he knows of no such case from his follow-up records. Glycosuria, except when regarded as due to diabetes before operation, disappeared after operation. These results are stressed since such patients are not subjected to diabetic management; not only are carbohydrates not restricted in the diets of such patients, but they are encouraged. The histories alone may be suggestive but it may here be observed that one is not justified in drawing conclusions from them for the following reasons:—

To conclude, in a given case, that diabetes was caused by hyperthyroid-

ism, it is important to definitely demonstrate that the individual was not a potential or mild diabetic prior to the onset of the hyperthyroidism. Histories, carefully, as they may be taken, are misleading. In potential, and in the early stages of chronic progressive, diabetes, as is generally recognized, there are, as a rule, no signs or symptoms. The glycosuria is usually discovered accidentally during the course of a routine examination for life assurance or for some other purpose. It is, also, generally recognized that potential diabetes may be made active and mild diabetes may be converted temporarily or even permanently into a severe form, by an injury, operation or any other illness. Does this explain the diabetes which developed subsequently to operation for hyperthyroidism in the cases referred to by Joslin[4]?

Evidence Based Upon Blood and Urinary Sugar Data

Soon after the introduction of thyroid preparations in medicine, Dale James[15] in 1894 first pointed out that their continuous use led to the appearance of sugar in the urine and that the sugar promptly disappeared on the drug being discontinued. In his "Zuckerkrankheit" von Noorden refers to the frequent occurrence of this form of glycosuria; but does not attribute it to diabetes. He believes that thyroid feeding merely elicits the presence of a pre-diabetic condition. Though hyperthyroidism, particularly Graves' disease, and conditions which result from administration of thyroid preparations are not exactly similar, a large part of the signs and symptoms of hyperthyroidism can be duplicated by feeding these substances. This observation led to a series of investigations. The literature is quite extensive and stages of fundamental importance only will be referred to. The methods of investigation may be divided into four types, namely, (a) studies of glycosuria only, (b) blood sugar studies, (c) respiratory metabolism, and (d) combination of all three methods.

Wilder and Sansum[16] have shown that when glucose is injected intravenously at uniform rates, glycosuria occurs more readily in hyperthyroid than in normal individuals. Later, however, Wilder[2] pointed out that this does not prove that there is anything at fault with oxidation. As defective oxidation of carbohydrates is regarded as a fundamental disturbance in diabetes, it cannot be concluded from these results alone that an individual is suffering from this condition. John takes exception to this view, as during these experiments, blood sugar data were not obtained. "The conclusion" he contends "is valid only if it can be proved that in the cases of hyperthyroidism in which glycosuria appears, only the permeability of the kidney for sugar is changed." In other words, it is implied that if hyperglycemia accompanies these experiments, the individual has diabetes.

Just as it is difficult to interpret results of physiological experiments where urinary sugar only is studied, so are difficulties met with clinically. Blood sugar studies are essential; but, as will presently be shown, their interpretation is not simple; in hyperthyroidism, the blood sugar may be very misleading.

About a decade ago, prior to the presently available bedside facilities for basal metabolic rate determinations, blood sugar time curves were widely made use of in the diagnosis of hyperthyroidism. These tests were based upon the fact that the glycosuria of hyperthyroidism depends upon hyperglycemia. As hyperglycemia precedes glycosuria (in the absence of the low renal threshold) the value of its detection is obvious. In the majority of cases, however, in the absence of diabetes, hyperglycemia is very uncommon when bloods are collected in the fasting state. Blood sugar time curves were, therefore, made use of. It is generally recognized that following glucose ingestion, blood sugar time curves may detect abnormal carbohydrate metabolism long before there is hyperglycemia in the fasting state.

The curves obtained in hyperthyroidism are not unlike those found in diabetes, in so far as the maintained elevation of the blood sugar is concerned. The first extensive report of such curves was that of Denis, Aub and Minot[17] in 1917. The results obtained, when correlated with the clinical conditions, were not uniform. Though, following either thyroidectomy or other therapeutic measures which led to relief, the blood sugar levels tended to be lower, there was no definite relationship between the levels and the basal metabolism. These authors did not regard these abnormal curves as indicative of diabetes. Since then a large number of similar observations have been made by different workers with varying results. Characteristic findings may be seen in one of our most recent cases.

It will be noted that as the degree of hyperthyroidism decreased, as measured by the basal metabolic rate, there was also improvement of carbohydrate metabolism; when the basal metabolic rate was +50 per cent not only was there a mild grade of hyperglycemia in the fasting state but, at the end of two and one-half hours, there was still marked elevation of the blood sugar; whereas, seventeen days later when the basal metabolic rate had decreased to +28 per cent, not only was the blood sugar in the fasting state normal, but it was also normal at the end of the test. There was, however, hyperglycemia at the end of the two hour period, though of a much lesser degree than at the first test.

Valuable as such data may have

Hosp. No. 2806/30

May 28th: B. M. R. +50 per cent

Fasting	0.128 per cent
30 minutes after ingestion	0.212 per cent
60 " " "	0.256 per cent
120 " " "	0.312 per cent
150 " " "	0.285 per cent

June 14th: B. M. R. +28 per cent

Fasting	0.119 per cent
30 minutes after ingestion	0.217 per cent
60 " " "	0.238 per cent
120 " " "	0.188 per cent
150 " " "	0.109 per cent

been prior to the era of routine basal metabolic rate determinations for the diagnosis of hyperthyroidism, they are of relatively little value in order to settle the problem as to whether glycosuria found in a given case of hyperthyroidism is, or is not, of diabetic origin. According to John such curves suffice, since, to quote verbatim "Hyperglycemia is the result of faulty oxidation of glucose." This view expressed will, again, be referred to. Direct proof, however, that in hyperthyroidism, in the absence of true diabetes, there is no defective oxidation of carbohydrates may be found in the experiments first recorded by Du Bois[18], then by Sanger and Hun[19], by Richardson[20] and later by Marsh[5]. These observations clearly demonstrate that not only are individuals suffering from hyperthyroidism able to oxidize carbohydrates as readily as a normal individual, but they apparently utilize sugar with marked avidity. In the cases reported there was no glycosuria with ordinary diets.* That individuals with hyperthyroidism also oxidize carbohydrates very readily even when they manifest hyperglycemia and glycosuria, in the absence of diabetes, may readily be seen from one of our cases recorded in Table 1. The data represent respiratory metabolism and blood sugar time curves obtained simultaneously following the ingestion of 100 grams of glucose.

This is our routine procedure in cases of glycosuria of doubtful origin. Though the data appear formidable, the technique, once it is perfected, is simple. As the details were previously reported in a study of renal glycosuria[21], and for purposes of brevity, they will not be repeated here. An observation may, however, here be made with regard to the calculation of the non-protein respiratory quotients.

For the calculation of the non-protein respiratory quotients, the urines are not collected periodically, as this, from experience, has been found to be impossible, unless the individual has marked polyuria or is given large quantities of water. The latter procedure, however, leads to the washing out of stored nitrogen and the error from such practice may be much greater than when one sample of urine is obtained at the end of the test and the amount of nitrogen excreted per hour is calculated on the assumption of a uniform rate of excretion. With the latter procedure, there is also a lesser tendency to disturb the patient—a very important matter in respiratory work.

Briefly, the data in Table 1 demonstrate that, in hyperthyroidism, without diabetes, there is no disturbance of carbohydrate oxidation, in spite of hyperglycemia and glycosuria. As a matter of fact, in this particular case, carbohydrates were oxidized very rapidly, when hyperglycemia was at its maximum. This is shown by (a) the respiratory quotients, (b) the rate of oxidation of glucose (grams per hour) and, (c) the percentage increase of heat production above the basal level (specific dynamic action).

It is interesting here to note the high urinary nitrogen. During a period of three hours, with no intake of nitrogen,

*In five of the cases investigated by Sanger and Hun, glycosuria was found only after glucose ingestion. In Case No. 5 studied by Du Bois, a trace of sugar was found on one occasion only.

there was an excretion of 1.26 grams or approximately 10 grams per twenty-four hours. This is a characteristic of hyperthyroidism and is found only in diabetes when there is marked emaciation or acidosis. In this case, there was marked emaciation, but no acidosis. With marked emaciation in diabetes, however, one would not observe such high respiratory quotients and, in the absence of treatment, the blood sugar would certainly not be normal in the fasting state.

Data of the nature just presented including the work of such authorities as Du Bois and Richardson are not however acceptable, according to John, as proof of the absence of diabetes. This is shown by the following explanation, as suggested by John, for the above mentioned results.

"This one would expect, for if the total oxidation of the body is increased in cases of hyperthyroidism, as is shown by the high metabolic rate, then the rate of combustion of carbohydrate must also be increased. Moreover, this higher rate of combustion of carbohydrate will continue until the islands of Langerhans can no longer supply a sufficient quantity of insulin to cope with the increased demand. In other words, in hyperthyroidism there is a hyper-secretion of insulin which lasts as long as the islands of Langerhans can stand the demand on them. In the early stage of hyperthyroidism, as is stated by these authors, there is only this increased metabolic function, a sort of last rush of flames before the fire dies down. Carbohydrate (and protein and fat as well) are burning with a greater intensity, as the R. Q. curve shows, the R. Q. falling only at a later stage when the islands are becoming exhausted and are no longer able to supply a sufficient amount of insulin . . . etc."

I find it rather difficult to follow the above arguments. The rapid oxidation of carbohydrates, it is stated, is to be expected if the total oxidation of the body is increased; if the rate of metabolism is increased, then the rate of combustion of carbohydrates must also be increased. This view does not conform to experience; the rate of metabolism and the rate of oxidation of carbohydrates in uncontrolled diabetes, that is, when glycosuria is present, have never been found, according to the literature, to be parallel. Another view, it will be noted, is that the falling respiratory quotient in the late stages of hyperthyroidism is an index of the exhaustion of the islands of Langerhans. Low respiratory quotients are undoubtedly found in advanced cases of hyperthyroidism. These, however, may be readily explained on the basis of exhaustion of glycogen reserve rather than defective carbohydrate oxidation. Proof of this may be seen in Table 2. This was a case of severe hyperthyroidism without glycosuria. It will be noted, following glucose ingestion, that there was a marked rise of the respiratory quotients and increased utilization of carbohydrates. If the low quotient found in this case in the fasting state was due to exhaustion of insulin, such rates of oxidation of carbohydrates as found would hardly be possible.

It may be observed that in the two cases reported here (Tables 1 and 2) we have a possible explanation of the occurrence of glycosuria in one case of hyperthyroidism and its absence in

TABLE I.

RESPIRATORY METABOLISM AND BLOOD SUGAR TIME CURVE OBTAINED SIMULTANEOUSLY FOLLOWING GLUCOSE INGESTION IN A CASE OF MARKED HYPERTHYROIDISM (HYPERPLASTIC TYPE) WITH GLYCOSURIA.

Hosp. No. 4896/27. Female. Age 39 years.

Period	Respiratory Exchange		Respiratory Quotient		Calories per hour.	Percentage increase of calories above basal.	Grams carbohydrate oxidized per hour.	Blood sugar per cent.
	O_2 Consumption (litres)	CO_2 (litres)	Total	Non-protein.*				
Fasting	14.83	13.05	0.879	0.893	71.80		9.5	0.111
	GIVEN 100 grams of glucose in 250 cc. water flavoured with lemon juice.							
30 min. later	16.52	15.01	0.908	0.930	80.79	12.5	15.4	0.166
60 min. later	15.79	15.12	0.957	0.985	77.98	8.6	15.6	0.250
120 min. later	16.12	14.87	0.922	0.943	78.97	10.0	13.5	0.232
180 min. later	16.00	14.54	0.908	0.927	78.19	8.8	12.8	0.178

* Urinary nitrogen = 1.26 grams in 3 hours.

TABLE 2.

RESPIRATORY METABOLISM AND BLOOD SUGAR TIME CURVE OBTAINED SIMULTANEOUSLY FOLLOWING GLUCOSE INGESTION IN A CASE OF MARKED HYPERTHYROIDISM (HYPERPLASTIC TYPE) WITHOUT GLYCOSURIA.

Hosp. No. 6075/25. Female. Age 34 years.

	Respiratory Exchange		Respiratory Quotient		Calories per hour.	Percentage increase of calories above basal.	Grams carbohydrate oxidized per hour.	Blood sugar per cent.
	O_2 Consumption (litres)	CO_2 (litres)	Total	Non-protein.*				
Fasting	13.89	10.84	0.780	0.774	65.39		2.9	0.078
	GIVEN 100 grams of glucose in 250 cc. water flavoured with lemon juice.							
30 min. later	15.62	13.57	0.868	0.880	75.38	15.2	9.3	0.200
60 min. later	16.78	14.79	0.881	0.896	81.40	24.3	11.4	0.252
120 min. later	14.97	13.65	0.911	0.936	73.08	11.8	12.1	0.166
180 min. later	15.21	14.44	0.949	0.981	74.88	14.8	14.3	0.133

*Urinary nitrogen = 1.42 grams in 3 hours.

another and also an explanation of the lack of parallelism noted at times between the levels of blood sugar time curves and rates of metabolism. A fundamental difference, according to Allen, between the glycosuria of hyperthyroidism and that of diabetes, is that though in both cases, glycosuria depends upon hyperglycemia, in diabetes the glycosuria is independent of the glycogenic content of the liver. In other words, unlike in diabetes, in order to produce glycosuria in hyperthyroidism, the patient must have a good store of glycogen. Since the storage of glycogen tends to be exhausted in severe cases and in cases of long duration, one would expect, in such cases, a high metabolic rate and no glycosuria; whereas, with hyperthyroidism of short duration one may expect a parallelism between the glycosuria or level of the blood sugar time curve and the basal metabolic rate, as the glycogen reserves have had relatively less time to be exhausted.

Respiratory data add further proof that the glycosuria of hyperthyroidism is not the same as that of diabetes. In diabetes, there is not only evidence of defective oxidation of carbohydrates, but there is much to suggest that storage of carbohydrates is also at fault. If, therefore, it can be shown that the glycosuria of hyperthyroidism is the result of defective storage, one might then suggest a causal relationship between the two conditions. Sanger and Hun[19] unable to explain their experimental results on the basis of defective oxidation, suggested defective storage. It is, therefore, interesting here to note the recent observations of Richardson, Levine and du Bois[22]. By an ingenious experiment, these authors have been able to demonstrate that defective storage of glycogen need not be made use of as an explanation of the blood sugar time curves in hyperthyroidism. The glycogen reserves of two patients suffering from exophthalmic goitre were studied and were estimated to be at least as great as normal. Evidence was presented against the theory that there is any defective mechanism by which glycogen is stored in this condition. These authors suggest that the blood sugar time curves observed might be explained on the basis of unusually rapid or complete absorption of sugar from the intestines or to a temporary increase of glycogenolysis. Having, therefore, eliminated both defective storage and defective oxidation to account for the glycosuria of hyperthyroidism, there is little left of an experimental nature to support the view that there is a causal relationship between this disease and diabetes.

As the above conclusion is based practically upon the identical data made use of by John, it is obvious that the different conclusions are not the result of experiment, but of interpretation. It is, therefore, necessary to find wherein there is disagreement. This is clearly shown in John's interpretations of his own blood sugar curves and in his criticisms, particularly of the work of Wilder and Sansum, of Sanger and Hun and of Marsh. The presence or absence of hyperglycemia appears to be the critical differentiating point between diabetic and non-diabetic glycosuria; hyperglycemia and diabetes are apparently regarded as synonymous. Thus, with regard to blood sugar curves, it is stated, to quote verbatim,

"I cannot but feel that a protracted hyperglycemia after the ingestion of a large dose of carbohydrate means that the body is unable to supply insulin in sufficient quantity to transform this carbohydrate into glycogen to be stored in the liver and muscles, and bring about its proper oxidation," and, again, "A study of tolerance tests shows a range of response from the perfectly normal to that which *indicates* the presence of severe diabetes. There is no definite line of demarcation between the normal and the diabetic state, and no matter where one might put a dividing line, *the high incidence of diabetes would still be evident.*" "Hyperglycemia," John insists, "is the result of faulty oxidation of glucose in the body" and his criticism of Marsh's work is particularly worthy of note here. Marsh, because of his simultaneously determined respiratory metabolism and blood sugar time curves does not attribute the hyperglycemia and glycosuria noted to defective oxidation of carbohydrates. With regard to this, John makes the following observations: "If we are to accept Marsh's conception, where are we to draw the line between diabetic and non-diabetic hyperglycemia and glycosuria"? and, later on, "Why does Marsh advocate the glucose tolerance test as a means of differentiating the thyroid glycosuria from diabetic glycosuria and then disregard his own figures"? With regard to the latter conclusion, it is obvious, at least to the writer, that Marsh's purpose in reporting the particular case referred to was to demonstrate that, in exophthalmic goitre, even when hyperglycemia is at its maximum, oxidation of carbohydrates, unlike in diabetes, may also be at a maximum.

Interpretation of Blood Sugar Data

An important fact which appears to have been overlooked by John is that with blood sugar time curves as with other laboratory tests, a variety of conditions may be responsible for similar results. Interpretation of laboratory tests depends upon recognition of underlying physiological principles. It is quite true that hyperglycemia is a characteristic response to the ingestion of glucose in diabetes. Hyperglycemia is, however, also, found in conditions other than diabetes and there is much evidence that in these conditions and in diabetes the mechanism of its production is not the same. For example, hyperglycemia and glycosuria may be produced in normal individuals by the injection of adrenalin and, when hyperglycemia is at a maximum, respiratory metabolism data clearly demonstrate that carbohydrates are being oxidized very readily.* This is contrary to experiences with diabetes. Allen's[23] observations with regard to adrenalin may here be referred to. "With adrenalin glycosuria, much of the injected dose of dextrose may be utilized at the height of the glycosuria and the utilization increases with increase of dose . . . The glycosuria is not a diabetes and does not depend upon the inhibition of the pancreas nor upon neutralization, destruction or inefficiency of the internal pancreatic secretion." This Allen states also implies to the thyroid.

Adrenalin is particularly mentioned as an example, because the writer is of the opinion that many of the signs and symptoms of hyperthyroidism are due to this internal secretion. There is much to support this view. Excess

*Unpublished data.

quantities of adrenalin in the circulation have been reported and some of the signs and symptoms of hyperthyroidism are not unlike those following adrenalin injection, namely, the mental confusion, tachycardia, palpitation, glycosuria and the peculiar pulse pressure-pulse rate relationship. The latter phenomenon is particularly worthy of note. As is well known, injection of adrenalin results in an increased pulse rate accompanied by increased pulse pressure. As far as the writer is aware, an increased pulse pressure accompanied by an increased pulse rate is found in hyperthyroidism only, if we exclude aortic disease and congenital or other cardio-vascular abnormalities (arterio-venous aneurism, etc.).

Application of Allen's Paradoxical Law to Diagnosis

Simultaneously determined respiratory metabolism and blood sugar time curves, because of the technique involved have obviously limited use, as such curves can be made use of in hospital practice only. They represent part of our routine procedure in the diagnosis of doubtful cases of glycosuria. A much simpler procedure, however, and equally reliable, in our experience, is the application of Allen's Paradoxical Law. Briefly, this Law is that the more sugar is given to non-diabetic individuals, the more is utilized. As Allen puts it, "Limits of tolerance in non-diabetic animals are all apparent, not real; there is no real limit of the power of utilization of sugar, except death . . . The Paradoxical Law of dextrose distinguishes sharply between diabetic and every type of non-diabetic animals. The limits of tolerance in diabetic animals are real and not apparent. In totally diabetic animals, an injection of dextrose causes an increment of glycosuria not only equal to, but frequently greater than, the injected dose. In milder diabetes, not only is the proportion of excreted to injected dextrose generally high, but the assimilation may be made worse instead of better by an overdose—just the opposite of the Paradoxical Law." Allen[23] first suggested that this Law may be found of service to clinical tests of diabetes and suggested that it is probably more specific for decision between active diabetes and other forms of glycosuria which may imitate it, than detecting incipient diabetes in its earliest stages. In our routine, the individuals are given diets of constant composition with respect to protein and fat and the amounts of carbohydrates are increased daily by the administration of glucose in small amounts at frequent intervals. An example is shown in Table 3.

J.A., a male, (Hosp. No. 3475/29), age 53 yrs., was referred to the department of metabolism by Dr. R. R. Fitzgerald on July 3rd, 1929. He was suffering from hyperthyroidism and manifested the typical signs and symptoms of exophthalmic goitre. There was a history of glycosuria prior to his admission. On account of the latter, a blood sugar time curve was obtained with the following results:—

Period	Blood Sugar	Urine Sugar
Fasting	0.113 per cent	0
30 minutes after ingestion	0.217 " "	+
60 " " "	0.263 " "	++
120 " " "	0.181 " "	trace
150 " " "	0.161 " "	0

TABLE 3.

DIET DEMONSTRATING ALLEN'S PARADOXICAL LAW.

Hosp. No. 3475/29. Male. 53 years.

Date	URINE			B. M. R.	Blood sugar (fasting) %	DIET.			Remarks
	sugar	acetone bodies	nitrogen			COH	Fat	Prot.	
July 5th						125	150	60	
6th	+	tr		+56		125	150	60	Lugol's iodine 0.5 cc. t. i. d.
7th	tr	tr				125	150	60	
8th	tr	tr			0.133	125	150	60	
9th	tr	0				125	150	60	
10th	0	0	12.5			225	150	50	Glucose 10 gms. every hour for 10 hours
11th	tr	0	11.5		0.117	325	150	50	Glucose 20 gms. every hour for 10 hours
12th	tr	0	9.8	+33		325	150	50	Glucose 20 gms. every hour for 10 hours
13th	tr	0	5.3?		0.119	425	150	50	Glucose 30 gms. every hour for 10 hours
14th	0	0				425	150	50	Glucose 30 gms. every hour for 10 hours
15th	tr	0	6.73			425	150	50	Glucose 30 gms. every hour for 10 hours
16th	0	0		+16	0.114	425	150	50	Glucose 30 gms. every hour for 10 hours
17th	0	0				425	150	50	Glucose 30 gms. every hour for 10 hours
18th	0	0				425	150	50	Glucose 30 gms. every hour for 10 hours
19th	0	0		+10	0.129	425	150	50	Glucose 30 gms. every hour for 10 hours
20th	0	0				425	150	50	Glucose 30 gms. every hour for 10 hours
21st	0	0				425	150	50	Glucose 30 gms. every hour for 10 hours
22nd	0	0				425	150	50	Glucose 30 gms. every hour for 10 hours

On admission, there was, again, glycosuria and, as there was no acetonuria, Allen's Paradoxical Law was applied. Observations were made with regard to the relationship between (a) intake and output of sugar, (b) glycosuria and nitrogen excretion, and (c) glycosuria and basal metabolism.

As pointed out before, nitrogen excretion may be markedly increased in these cases. However, if the individual can oxidize glucose very well, that is, if he is not a diabetic, the administration of large amounts of glucose will tend to have a protein sparing effect and thus cause a decreased excretion of nitrogen. Should the glycosuria be due to diabetes, the same effect can be obtained only with the use of insulin. The following are to be noted (Table 3).

(a) No relationship whatever between the intake and excretion of sugar; as a matter of fact, traces of sugar only were found when the diet was increased to 425 grams of carbohydrate daily.

(b) In spite of huge quantities of carbohydrates, the blood sugars were persistently normal in the fasting state, except on one occasion (July 8th, 1929) when there was a mild grade of hyperglycemia, namely, 0.133 per cent.

(c) Sugar had a protein-sparing effect *when the basal metabolic rate was still above normal.* The daily intake consisted of approximately 8 to 9 grams of nitrogen. It will be noted that up to July 12th, the excretion was greater than the intake; the body proteins were being conserved.

Beyond the last date recorded in the Table, the case is of no further interest with respect to the subject matter. A thyroidectomy was performed and the patient made an uneventful recovery.

Summary

The conclusion which the writer draws from all of the above observations is that the glycosuria of hyperthyroidism is not of diabetic origin. Clinical experience alone, however, would appear to suffice, in order to draw this conclusion, as the glycosuria of such individuals disappears after successful management of the hyperthyroidism. This finding is stressed, in view of the fact that not only are such patients allowed unrestricted diets, but large quantities of carbohydrates are actually encouraged. This would, obviously, not be the course of a potential or active diabetic when exposed to such treatment. It is hardly necessary, however, to point out that, glycosuria, when met with in case of hyperthyroidism, should always be given serious consideration, as amongst such individuals there may be true diabetes. Simultaneously determined respiratory metabolism and blood sugar time curves and the application of Allen's Paradoxical Law help in the differential diagnosis.

References

[1]Fitz, R.: Arch. Int. Med., vol. 27, p. 305, 1921.

[2]Wilder, R. M.: Arch. Int. Med., vol. 38, p. 736, 1926.

[3]John, H. J.: Endocrinology, vol. 11, p. 497, 1927.

[4]Joslin, E. P.: Treatment of Diabetes, 4th Ed., (Lea and Febiger) 1928.
[5]Marsh, P. L.: Ann. Clin. Med., vol. 4, p. 1012, 1926.
[6]Holst, J.: Act. Med. Scand., vol. 55, p. 302, 1921.
[7]Rohdenberg, G. L.: Endocrinology, vol. 6, p. 519, 1922.
[8]Garrod, A. E.: Lancet, vol. 1, pp. 483, 557, 629, 1912.
[9]Marinesco, G. and Parhon, C.: Comp. rend. Soc. de biol., vol. 64, p. 768, 1908.
[10]Falta, W.: Wien. klin. Wchschr., vol. 22, p. 1059, 1909.
[11]Lorand, A.: Comp. rend. Soc. de biol., vol. 56, p. 488, 1904.
[12]Shields, Warren: The Pathology of Diabetes Mellitus, (Lea and Febiger) 1930.
[13]Burns, J. H. and Marks, H. P.: Jour. Phys., vol. 60, p. 131, 1925.
[14]Bodansky, A.: Proc. Soc. Exp. Biol. and Med., vol. 21, p. 46 and vol. 20, p. 538, 1923.
[15]James, Dale: Br. Jour. Derm., quoted by Cammide and Howard, New Views on Diabetes Mellitus (Oxford) 1923.
[16]Wilder, R. M. and Sansum, W. D.: Arch. Int. Med., vol. 19, p. 311, 1917.
[17]Denis, W., Aub., J. C. and Minot, A. S.: Arch. Int. Med., vol. 20, p. 964, 1917.
[18]Du Bois, E. F.: Arch. Int. Med., vol. 17, p. 915, 1916.
[19]Sanger, B. J. and Hun, E. G.: Arch. Int. Med., vol. 30, p. 397, 1922.
[20]Richardson, H. B.: Erg. d. Physiol., vol. 24, p. 588, 1925.
[21]Rabinowitch, I. M.: Quart. Jour. Med., vol. 17, p. 260, 1924.
[22]Richardson, H. B., Levine, S. Z. and Du Bois, E. F.: J. Biol. Chem., vol. 67, p. 737, 1926.
[23]Allen, F. M.: Glycosuria and Diabetes (Harvard), 1913.

Extra-Insular (Central) Glycosuria With Hyperglycemia Following Epidemic Encephalitis

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SINCE the epoch-making discovery of von Mering and Minkowski[1] in 1889 that a lesion in the islands of Langerhans is responsible for diabetes mellitus and the much more recent discovery of Banting and Best[2] that insulin has a favorable effect on this condition, the tendency to ascribe every case of glycosuria and hyperglycemia to either functional or pathologic changes in the islands of Langerhans has been pronounced. However, it is possible for these conditions to occur without involvement of the islands of Langerhans and we feel that when one encounters such a case of hyperglycemia or glycosuria of non-insular origin it is of sufficient interest to be reported. The differentiation between the two is not a purely academic matter. It is highly important from both the prognostic and the therapeutic standpoint.

Case Report

Mrs. R. C., age 37, was admitted to the Beth Israel Hospital, June 6, 1929.

Chief Complaints: Dizziness, generalized swelling, elimination of great quantities of urine and excessive thirst accompanied by bitterness and dryness in the mouth.

Past History: Two abortions, one two years before admission, the other one year before admission. The patient had one child (8 years old) in a marriage of ten years. Past history otherwise unessential.

Present Illness: According to the history given by the family physician, Dr. H. Lesser, who referred the case to the hospital, the patient became ill one month before admission. She had had symptoms of a mild infection interpreted as influenza and from which she apparently recovered. A few days later, however, she began to complain of dryness of the mouth and extreme thirst that compelled her to partake of excessive fluids and void large quantities of urine. A generalized swelling of the face and body appeared, especially noticeable over the extremities. This diminished somewhat while she was confined to bed. She became drowsy, sluggish, weak and dizzy. Her skin became coarser in texture and darker in color. There was a generalized eruption, particularly over the face, chest and back. The patient was sent into the hospital with the diagnosis of diabetes mellitus with impending coma.

Physical Examination: The patient is a well developed, obese woman lying comfortably in bed, well oriented and co-operative. Her scalp is dry with thinning hair. Her face shows diffuse eruptions, chiefly of discrete, small papulopustular lesions with reddish areolae, extending down onto the chest anteriorly and posteriorly. The skin, generally, is very rough and is dark in hue. The dependent parts, like the breasts, and extremities show cutis marmorata. The skin lesion was diagnosed by Dr. Oscar Levine as hydrocystoma and folliculitis.

Examination of the mouth revealed mild pyorrhea, particularly around the capped teeth; the tongue was coated; the throat congested; the thyroid was not palpable and there was no adenopathy. Both malar regions

were prominent due to swelling of the soft tissues. Chest examination was negative. The heart was slow and regular. Blood pressure was 154/76. Palpation of the abdomen showed a slight enlargement of the liver, but it was otherwise negative. The edema was not a pitting one but was very hard and tense. In the presence of a dry skin, it gave the impression of the type encountered in myxedema. There was no pallor of the skin, which was rather uniformly dark brown and extremely rough. There was no girdle obesity. The reflexes were normal except for diminished knee jerks. The pupils were equal, regular, and reacted to light and accommodation. There was no disturbance of vision; the eye-grounds and field of vision were normal, as confirmed by Doctors Torok and Slomka. A complete neurologic examination by Dr. E. P. Goodhart was negative. The temperature varied from 99° to 101°, being lowest at 6 A. M., highest at 2 P. M. On certain days it rose transiently to 102° and 103°. The pulse varied from 70 to 100. The blood pressure varied from 150/100 to 80/60 except on June 29, 1929, when in the preagonal state it dropped to 80/14.

Laboratory Findings: The urine varied in amount from 45 to 200 ozs. daily. The specific gravity fluctuated from 1010 to 1026. The albumin never exceeded +; glucose varied from 0 to ++++. There were no definite microscopic findings. (See Charts I and II).

The blood count showed on the average:

Hemoglobin	75%
R. B. Cells	4,100,000
W. B. Cells	8,000-18,000
Diff. Count:	
Segmented	84%
Staffs	4%
Small lypmhs.	10%
Monos	2%
Platelets	166,400

The blood sugar varied as recorded, Charts I and II. The blood chemistry showed nonprotein nitrogen: 29.0 mgms. per 100 cc. of blood; cholesterol 158 mgs.; chlorides 478;

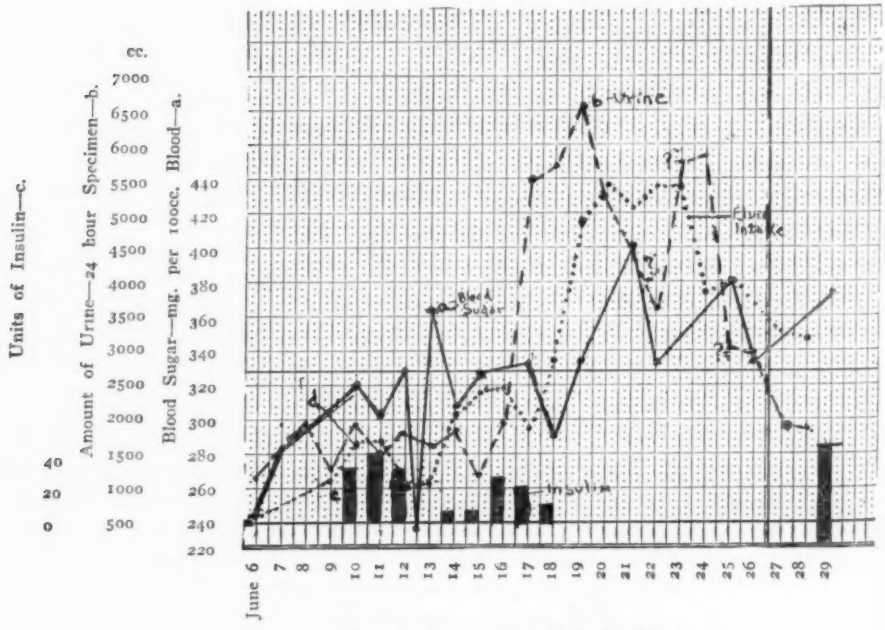

Chart 1. a ———— Blood Sugar.
b — — — 24 hour Urine Specimens.
d . . . . Fluid Intake.
c ▬▬▬ Units of Insulin.

calcium 9.8; total proteins 6.80; serum albumin 4.26; serum globulin 2.54; ration of albumin to globulin 1.6 normal. The blood Wassermann was negative. The cerebrospinal fluid on June 28, 1929, was under normal pressure, 8 mm. It was clear in color, showed albumin +, globulin slight trace, reduction of sugar 0.114; cells per cu. cm. 1 and lymphocytes; negative Wassermann. Basal metabolism on June 13 was +49, the patient being very excitable. On June 15 it was +11. X-Rays of skull, long bones and chest were negative. The electrocardiographic tracings showed inverted T waves in Leads II and III.

Treatment

In view of the above findings and the history, the patient was placed on a diet of 1000 cc. of milk per diem to determine her carbohydrate tolerance. Despite this low diet, her blood sugar rose to 284 mgms. per 100 cc. of blood, and the urinary findings were sugar +++, acetone +. On the day after admission a 24-hour specimen of urine showed 1.7% sugar (32 grams). The patient was kept on this diet for four days, during which time she showed persistent glycosuria. The diet was then changed to 1000 cc. buttermilk, and vegetables. The blood sugar rose two hours after breakfast to 320 mgms.

On June 10, 1929, four days after admission the patient was given 30 units of insulin with a change of diet to carbohydrates 40, proteins 40, fat 100, making a total of 1220 calories, and yielding 73.2 grams of glucose. The blood sugar before the meal was 307 mgms. During the afternoon the patient received an additional 20 units of insulin with a repetition of the dose in one hour. During this time she complained of dryness of the throat, weakness, and pain in the legs. (See Chart II, June 11).

On June 12, while the patient was still on the diet instituted the day before the blood sugar two hours after breakfast (11 A. M.) showed 330 mgms. Because of the high blood sugar findings, the patient was given 15 units of insulin at 1:50 P. M. At 2 P. M. the urine showed a trace of albumin and a trace of sugar. At 3:30 P. M. (1½ hours later) she complained of dizziness, became irrational, talkative, noisy and was transiently violent and had to be restrained. The urine at this time showed albumin +++, sugar ++++, acetone ++, and the blood sugar was only 235 mgms.

On June 13 she was given 3 ampules of infundin at the suggestion of Dr. Evan Evans. The next morning at 2 A. M. (June 14) she became restless, talkative and dizzy. The blood sugar rose to 363 mgms. without insulin. (See Chart II)

The patient was placed on diets varying from a low to high carbohydrate ratio to ascertain if the blood sugar level would vary in direct proportion to the carbohydrate intake. Occasionally insulin was given to determine its effect on the blood sugar. The variations in doses of insulin administered together with the blood and urinary findings are shown in Chart I. On the day before exitus there was an acetone breath, high blood sugar. Twenty units of insulin were given on two occasions during the day. The patient became drowsy, very weak, and refused all food. There was no Kussmaul breathing and when death came, June 29, 1929, it was very sudden. There was an abrupt cessation of breathing and heartbeat indicative of vagus paralysis.

Diagnosis

From the history of glycosuria accompanied by an increase in body weight, headache, dizziness and the fact that the symptoms of an acute infection had been present for several days, we were impressed by the fact that we were not dealing with diabetes mellitus but more likely with a hyperglycemia and glycosuria of a post-encephalitic lesion in the thalamic region. The progress of the disease with the non-response to the treatment of diabetes seems to have verified our original contention. The diabetic regime and the insulin injections even in the smallest doses brought about extraordinary mental reactions. The patient became very abusive, maniacal, and

CHART II:—CALORIC VALUES OF FOOD WITH DAILY FLUID INTAKE AND OUTPUT—AS WELL AS BLOOD SUGARS AND INSULIN DOSAGES

		DIET						URINE							BLOOD		
DATE	FOOD INTAKE	CARBOHYDRATE	PROTEIN	FAT	TOTAL CAL'S	TOTAL GLUCOSE INTAKE	FLUID INTAKE	TOTAL GLUCOSE OUTPUT Gms.	TOTAL GLUCOSE OUTPUT %	SUGAR	ACETONE	DIACETIC	VOLUME IN C.C. 24 HRS.	CARBOHYDRATE BALANCE	BLOOD SUGAR IN MG. 100 cc.	INSULIN	REMARKS
1929 6/6	1000 cc. milk	48	32	32	608	–	–	–	–	+	0	0	1140	–	242	0	Dizziness
6/7	1000 cc. milk	48	32	32	608	68.0	–	–	–	+++	+	0	–	–	284	–	
6/8	1000 cc. milk	48	32	32	608	68.0	–	32.8	1.7	0	0	0	1935	–	–	–	Dizziness
6/9	1000 cc. milk	48	32	32	608	68.0	1020	21.9	1.7	–	0	0	1290	46.1	–	–	Dizziness
6/10	1000 cc. buttermilk & vegetable	60	36	–	440	81.6	1560	–	–	–	–	–	1920	–	320	30	
6/11	Diabetic Diet	40	40	100	1220	73.2	1560	–	–	–	–	–	1470	–	307	20–20	Dryness in Throat
6/12	Diabetic Diet	40	40	100	1220	73.2	1000	– –	– –	trace ++++	– ++	0 0	1800	–	330 235	15–15	Irrational, Talkative, 4 hours later
6/13	24 oz. milk	36	24	24	456	52.3	1020	44.8	2.8	trace	0	0	1600	7.5	363	–	Dizziness, Talkative
6/14	26 oz. milk	39	26	26	494	67.4	2040	–	–	trace	0	0	1860	–	307	5	Dizziness, Restless
6/15	24 ox. milk	36	24	24	456	52.3	2400	–	–	–	–	–	1200	–	323	5	Restless
6/16	Diabetic Diet	40	40	100	1220	73.2	2430	25.7	1.3	+	0	0	1980	47.5	–	10–10–5	Nervous
6/17	Diabetic Diet	40	40	100	1220	73.2	1830	54.9	1.0	+	0	0	5490	18.3	333	10–10	Irrational
6/18	Diabetic Diet	40	40	100	1220	73.2	2820	57.0	1.0	trace	0	0	5700	16.2	290	10	Restless
6/19	Diabetic Diet	40	40	100	1220	73.2	4860	65.4	1.0 1.0	marked trace	0 0	0 0	6540	7.8	333	–	Dryness in Throat Fair Day
6/20	Diabetic Diet	40	40	100	1220	73.2	5400	52.5	1.0	marked	0	0	5250	20.7	–	–	Intense Thirst, Drowsy

	Diabetic Diet	40	40	100	1220	73.2	5400	52.5	1.0	marked	0	0	5250	20.7	–	–	Intense Thirst, Drowsy
6/21	Buttermilk & Vegetables	60	36	–	440	81.6	5040	77.0	1.7	trace	0	0	4530	4.6	402	–	Fair
6/22	Buttermilk & Vegetables	60	36	–	440	81.6	5400	–	–	marked	0	0	3630?	–	333	–	–
6/23	Buttermilk & Vegetables	71	45	20	648	98.9	5400	97.4	1.7	trace	+	0	5730?	1.5	–	–	Restful
6/24	Buttermilk & Vegetables	71	45	20	648	98.9	3840	98.9	1.7	trace	+	0	5820	0	363	–	Drowsy
6/25	Buttermilk	30	19	12	308	42.0	3960	77.2	2.5	+		0	3090	35.2?	380	–	Sleepy, Vomiting
6/26	Buttermilk	24	16	0	160	33.0	–	–		+++	+	0	2940	–	333	–	Weak, Vomiting, Drowsy
6/27							3300	34.1	1.7	+	+	0	2010	–	–	–	Poor Day
6/28							3210	24.5	1.3	+++	+	0	1890	–	–	–	Vomiting
6/20										+++	+	0	–	–	374	20–25	Vomiting, Restless

slapped the resident in the face so that she had to be restrained.

Dr. Philip Horowitz saw this case during one of the mental reactions and advised a different brand of insulin, thinking the quality of insulin might have caused the reaction. However, smaller doses of another brand caused similar violent disturbances.

During the second week of the patient's stay in the hospital, her general condition improved slightly. However, the drowsiness persisted with eventual development of stupor. The general appearance, the findings of the skin, the falling out of the hair, the dyspnea, hyperglycemia and glycosuria persisted. Towards the end vomiting was constant.

Throughout the entire time and even shortly before death there was only + acetone. Even during the agonal period when she took no food at all and vomited excessively this remained so. At no time was there diacetic or oxybutyric acid.

From an analysis of the case it appears certain that it was not one of pancreatic or insular diabetes, but that the glycosuria and hyperglycemia were of central origin. The differential diagnosis lay in whether we were dealing with a tumor or hyperfunction of the anterior pituitary or metastatic or primary tumor of the hypothalamic region or a post-encephalitic sequela in the hypothalamic region. The pituitary lesion proper was ruled out by the negative eye examination. The normal eye grounds as well as the negative neurologic signs and the normal cerebrospinal fluid ruled out primary tumor of the brain spreading to the thalamic

region. With regard to metastatic tumor in the thalamic region, we are aware of the fact that despite the negative findings, such a lesion may have been present. Cases have been reported of metastatic tumor in the hypothalamic region or tuber cinereum as in a case reported by Futcher,[3] without any clinical evidence of a primary tumor. The complete x-ray examination of practically the whole osseous system and also of the lungs and mediastinum and the rapid course of the disease, in the case here reported, however, did not justify the suspicion of a metastatic tumor. On the other hand, the sudden onset of a febrile disease, diagnosed as influenza, followed by the symptoms described seemed to us to justify the diagnosis of glycosuria and hyperglycemia of central origin following epidemic encephalitis.

Discussion

In view of the fact that pathologic lesions are not readily demonstrable in diabetes mellitus, this affection was long considered a purely functional disorder. In 1855 Claude Bernard[4] began his search for an organic lesion to explain this important and widespread affection. He punctured the medulla at the level of the origin of the vagus and auditory nerves and succeeded in producing a definite glycosuria. This was brought about through the nerve fibers running to the liver by way of the hepatic plexus controlling the process of glycogenolysis. As a result of this important discovery, two schools arose, one consisting of those who believed every case of diabetes mellitus due primarily to a lesion in the sugar regulating center of the medulla oblongata (Piqûre diabetes) and the other that all cases of diabetes mellitus are of psychogenic origin and that Piqûre diabetes is due to psychic over-stimulation of the medulla oblongata.

Another step in the direction of demonstrating that lesions at the base of the brain may be responsible for diabetes was made in 1884 when Loeb[5] demonstrated that glycosuria and hyperglycemia are often associated with hyperfunction of the anterior lobe of the pituitary. Two years later Marie described a clinical entity known as acromegaly, resulted from anterior pituitary disease and frequently accompanied by hyperglycemia and glycosuria.

The relation of the pituitary gland to water and carbohydrate metabolism has continued to be a subject of interest in both experimental and clinical medicine. The most important and conclusive work has been furnished by Cushing and his pupils who demonstrated experimentally that hyperfunction of the anterior pituitary causes glycosuria and hyperglycemia. Their work has been confirmed by many experimenters. In view of the fact, however, that some experimenters have not obtained the same results as Cushing and that, clinically, in many cases of pituitary tumor or other forms of pituitary disease glycosuria is not present, and that the surgical removal in the human of the pituitary causes no disturbance in carbohydrate and water metabolism, it was natural for them to doubt the responsibility of the pituitary gland itself when diseased for disturbed carbohydrate metabolism, and to ask whether this responsibility may

not lie in the adjacent nerves or brain proper.

Light has been shed on this particular problem, by Cajal and Cushing,[6] Clara Kary,[7] Elmer, Kedzierski, and Scheps,[8] who have shown that the internal secretion of the pituitary gland is conducted by the nerve paths from the pituitary to the midbrain and thence to the third ventricle whence it eventually enters the circulation. This internal secretion of the pituitary gland gland has an inhibitory influence on the insular apparatus and produces a diminished insular secretion, thus interfering with utilization of carbohydrates and leading to hyperglycemia and glycosuria. Some experimenters have shown that injury to the nerves leading from the mid-brain does not in every case affect carbohydrate metabolism.

Brugsch, Dresel and Lewy[9] localized with greatest exactness the carbohydrate, water and salt metabolism centers in the hypothalamic region. They located two sugar centers in the floor of the fourth ventricle. The anterior one, at the oral end of the dorsal vagus islands . Irritation of this center leads to stimulation of the pancreas with an over-production of insulin and consequent hypoglycemia, a condition clinically described by Seale Harris,[10] and pathologically demonstrated by Wilder,[11] to be produced by adenoma of the islands of Langerhans.

Brugsch, Dresel and Lewy have shown that extirpation of the pancreas leads to secondary degeneration of the oral end of the dorsal vagus nucleus (anterior sugar center). These authors have shown a second sugar center, a caudal one, at the posterior end of the dorsal vagus nucleus. This is a sympathetic center sending its fibers by way of the jugular ganglion of the vagus and superior cervical sympathetic ganglion affecting the blood sugar level by way of the suprarenal glands. Irritation of the posterior sugar center leads to stimulation of the suprarenal glands with resulting hyperglycemia.

The work of these authors clearly and satisfactorily explains the experimental Piqûre diabetes of Claude Bernard, as well as the occurrence of glycosuria in some cases of apoplexy, basal meningitis, tumors of the base of the brain, metastatic tumors especially in the hypothalamic region, and the not infrequent disturbance of water, salt, carbohydrate and thermic metabolism encountered as sequelae of epidemic encephalitis.

The work of Brugsch, Dresel and Lewy has been verified by many experimenters and some clinicians, notably among them Eric Leschke.[12] Leschke goes so far as to attribute the disturbance in carbohydrate metabolism solely to a central origin, contending that all cases of diabetes mellitus are due to a functional or organic disturbance in the hypothalamic region, and that any co-existing lesion in the islands of Langerhans is merely secondary. In the vast number of cases according to Leschke an actual lesion of a carbohydrate center need not be present. A functional disturbance alone may suffice to inhibit the action of the islands of Langerhans by way of the sympathicus and thus bring about hyperglycemia and glycosuria. Just as E. Pick[13] of Vienna and H. Elwyn[14] of New York adhere to the conviction that salt and water metabolism dis-

turbances are entirely under the influence of the hypothalamic region, so is this claimed by Leschke for carbohydrate metabolism disturbance.

Enlightening as the results of the experiments of Brugsch, Dresel and Lewy, may have been, the recent work of Hiller and Tannenbaum[15] as well as of Hiller and Grinker[16] has cast great doubt upon those results. Hiller, Tannenbaum and Grinker have come to the conclusion that the carbohydrate disturbance brought about by the Brugsch-Dresel-Lewy experiments is not due to an actual hypothalamic lesion, but to certain technical errors in experimentation and in the interpretation of the experiments. They have shown that even ether anesthesia or manipulation of the head of an animal without causing a lesion in the hypothalamic region brings about glycosuria in the animal. They are skeptical as to whether any of the centers such as the salt and water centers are present in that location.

It is quite apparent that in most branches of medical investigation, especially regarding metabolism, the clinician must not be too much influenced by the results of contradictory experiments, else he cannot hope to escape confusion. It seems pretentious for one who himself has not partaken in the experiments to side conclusively with one or the other faction. The position of the clinician should, after all, be determined by clinical observation in a matter of contradictory experimental evidence. Clinically, it cannot be denied that cerebral lesions particularly those confined to the hypothalamic region, the pituitary proper and the connecting nerves between the pituitary and hypothalamic region, do give rise to disturbance in carbohydrate, water and salt metabolism. This was so well known long before the experimental era that it would mark a considerable step backward in clinical interpretation if one were to deny it simply on the basis of a recent contradictory experiment, no matter how authoritative the source of that experiment might be. It would be just as fallacious, however, if influenced by the experimental work demonstrating a metabolic center in the brain, one were to conclude that disturbance in carbohydrate, water and salt metabolism must in every case be traced to functional disturbance or to a pathologic lesion in the pituitary or in the hypothalamic region.

It is our opinion that every affection —organic or functional—and this concerns disturbances in metabolism more than any other disease, may originate either in the central nervous system, particularly in the vegetative centers, or in an organ proper. Regarding disturbance in carbohydrate metabolism, there is no doubt that purely functional disturbance of a non-progressive nature can and often does originate in the central nervous system or in a dysfunction of the thyroid or suprarenals. This form of carbohydrate disturbance is not synonymous with diabetes mellitus due to a disturbance of the islands of Langerhans. In reality, they are two independent affections.

In a state of health, the two centers —one central, the other peripheral— have an antagonistic activity. The posterior end of the dorsal vagus nucleus in the thalamic region stimulates the suprarenals causing a hyperglycemia

and equalizing the possible hyperglycemia from insular overproduction by the anterior center. If this equalization does not occur spontaneously, the administration of adrenalin brings it about. This is illustrated by the fact that hyperglycemia resulting from adenoma of the pancreas (Wilder) or hypofunction of the suprarenals (Addison's disease) is at least temporarily favorably influenced by adrenalin.

A co-affection of several organs concerned in the same process of metabolism, such as can be brought about by animal experimentation, is unlikely in the human unless chance or accident causes a rapidly destructive disease of one of these organs so that no time is given to the affected organ or to the organs with compensatory mechanism to adapt themselves to the situation. It is true that thyrotoxicosis, hyperadrenalemia and hyperfunction of the anterior pituitary lobe can produce glycosuria. However, in order for affection of these organs to lead to a permanent or true diabetes indicating that a co-affection of the islands of Langerhans is present to a degree that a diminished amount of insulin, or insulin of a less effective nature, is produced, rapidly destructive thyrogenic or suprarenal disease must be present, conditions only rarely encountered clinically. This is even more so in case of a hypothalamic lesion causing hyperglycemia and glycosuria. It is equally important to remember that a rapidly destructive disease of the islands of Langerhans such as is brought about by a cyst of the pancreas or syphilis of the pancreas may progress so rapidly as to affect the carbohydrate center in the thalamic region. The antagonistic functional activity of the hypothalamic region can not keep pace with the rapidly destructive process in the islands.

The clinical proof that glycosurias of non-insular origin not only co-affect the islands but most likely stimulate them to increased insulin secretion is demonstrated by the fact that glycosuria of hyperadrenalemia or hyperthyroidism or of functional or organic thalamic lesions are in most cases transient. But even if they persist—as in the case herein reported—neither the hyperglycemia nor glycosuria is aggravated by the additional intake of carbohydrates, nor is there a favorable influence exercised on the carbohydrate metabolism by the administration of insulin. Actually, as in our case again, insulin may be harmful. The patient has enough insulin so that the additional exogenous introduction serves as a definite stimulant to the insulin output and hyperinsulinemia results. Even where insulin is not directly harmful, the individual is refractory to it.

Clinical substantiation of the statement that disturbance of carbohydrate metabolism resulting from insular disturbance differs entirely from that of the extra-insular apparatus (hypothalamic, thyrogenous, suprarenal) is further provided by the fact that in the former the administration of carbohydrates fails to bring about an equal response of the islands in the output of insulin. Hence marked hyperglycemia and glycosuria occur. In "extra-insular" carbohydrate metabolism disturbance, the administration of carbohydrates stimulates, just as in the normal individual, the insular apparatus to additional insulin output. Con-

sequently there is no increase in the blood sugar and at most only a very slight increase in glycosuria. This is true, also, if the glycogenic function of the liver is disturbed and the liver does not store the glycogen either as a result of some inherent disease in the liver (hepatogenous glycosuria) or as a result of a disturbance in the thalamic center or suprarenals by way of the sympathicus. The excess of sugar in the blood stimulates the insulin apparatus to increased insulin output of effective quality so that the consequences of hyperglycemia or glycosuria, namely acidosis or diabetic coma, do not occur.

Von Noorden and Isaac[17] have described a form of glycosuria due to the excessive deposit of fat in the liver. Because of this excessive fat in the liver, it is impossible for glycogen to be deposited there. Hence the excess of sugar that is not deposited as glycogen passes out through the kidneys. These cases have no hyperglycemia unless very large quantities of carbohydrates are taken. Even then the hyperglycemia is only transient. Because of the lack of assimilation of the intake of carbohydrates the patient grows gradually weaker, although appearing strong. When disturbance in fat metabolism also sets in the patient becomes slowly acidotic, develops small quantities of acetone in the urine and becomes drowsy. This form of glycosuria differs from diabetes in those fat individuals where there is an excess of fat in the pancreas replacing the islands of Langerhans and thereby interfering with the output of insulin.

From what has been said, it seems almost paradoxical to group all cases of glycosuria and hyperglycemia as diabetes, or to insist that if one center of a cycle controlling metabolism is disturbed the others are necessarily coaffected. The reverse, in fact, is the case. If one center of carbohydrate metabolism is affected, the others come to the rescue in their accommodation as a compensatory mechanism. *We feel that an existing glycosuria and hyperglycemia indicate true diabetes mellitus only if the insular apparatus of the pancreas is defective.*

Should the affection lie in the thalamic center alone, or in the organs of internal secretion (thyroid, suprarenals or pituitary) the glycosuria and hyperglycemia are of the neurogenic type resulting from the sympathetic influence on the glycogenic function of the liver, in which case the islands of Langerhans are not—as stated by some authors—inhibited, but, in our opinion, are stimulated to greater insulin output in order to utilize the excess of carbohydrates and prevent acidosis.

In other words, the "extra-insular" carbohydrate metabolism by virtue of the endogenous excess of carbohydrates stimulates the insular apparatus to the production of insulin just as does an exogenous carbohydrate intake. Of course, it may be readily assumed that if such an endogenous carbohydrate excess exists — whether the cause be in the pituitary, thalamic center, liver, thyroid or suprarenals— it may exhaust the islands of Langerhans and even lead to their destruction and result in acidosis. It is possible, too, that is some cases of complete destruction of the islands of Langerhans, as may happen in a rapidly progressing pancreatic cyst or in syphilis

of the pancreas, over-stimulation of the compensatory centers may eventually lead to irritation and even to destruction of these centers, as is sometimes demonstrated in the acute animal experiment. This is clinically the exception.

Conclusions

A clinical case of extra-insular (central) hyperglycemia and glycosuria has been described. An effort has been made in both the description of the case and in the discussion not to confuse diabetes mellitus due to affection of the islands of Langerhans with hyperglycemia and glycosuria of extra-insular origin, be that origin central, thyrogenic, or suprarenal.

It is confusing to divide diabetes mellitus into insular and "extra-insular" groups. True diabetes is always insular. The "extra-insular" type spoken of by Umber,[18] which is refractory to insulin, is not true diabetes, but should be termed "extra-insular" glycosuria with or without hyperglycemia. In the insular type of diabetes, insulin exerts a favorable influence and in some cases the function of the islands can be entirely restored by its protracted use so that complete recovery results. It is well known and has again recently been further confirmed that in most cases of diabetes mellitus there are no demonstrable pathologic changes in the islands and that the disturbance is of a purely functional nature. The administration of insulin, therefore, spares the insular function and gives the islands a chance to recuperate and eventually return to normal.

In extra-insular glycosuria and hyperglycemia, on the other hand, the administration of insulin causes an increased output of endogenous insulin with the immediate effect of hyperinsulemia, which cannot be favorably influenced by the administration of carbohydrates or of adrenalin. The reason for this is that in insular diabetes the administration of carbohydrates or even of adrenalin does not bring about an extra production of insulin and hence the carbohydrates actually counteract the insulin shock. In extra-insular hyperglycemia or glycosuria, however, carbohydrates or adrenalin cause a greater output of insulin by the islands of Langerhans and are, therefore, harmful.

The administration of even the smallest doses of insulin in cases of extra-insular glycosuria, with or without hyperglycemia, especially originating in a disturbance in the pituitary or hypothalamic center, produces—as in our case—a violent mental reaction that is unlike the temporary manifestations of hyperinsulemia in insular diabetes, namely, marked weakness, cold perspiration and collapse manifestations, immediately relieved by the administration of carbohydrates or adrenalin.

There are, of course, cases of extra-insular hyperglycemia and glycosuria that behave very much like insular diabetes, terminating in acidosis. They are probably either complicated cases, or the central lesion may have been so severe and so rapidly destructive as to have actually led to secondary changes in the islands of Langerhans.

Many characteristics differentiate insular diabetes from extra-insular glycosuria with or without hyperglycemia. In addition to those already enumerated, it is important to remember that

true insular diabetes causes not only a disturbance in carbohydrate metabolism, but also a disturbance of fat and protein metabolism. This is not the case in extra-insular glycosuria with or without hyperglycemia.

BIBLIOGRAPHY

[1]v. Mering and Minkowski: Zentralbl. f. klin. Med. P., 393, 1889 and Arch. f. exper. Pahol. u Pharmakol., 26:371. 1889.

[2]Banting, F. G. and Best, C. H.: Amer. Journ. of Physiol. 59, 62, 63. 1922-1923.

[3]Futcher, T. B.: Amer. J. Med. Sci., Vol. 178, No. 6, P. 837, December, 1929.

[4]Bernard, Claude: Lecons sur la physiologie et la pathologie du systeme nerveux 1858; Lecons sur le diabete, 1877.

[5]Loeb, M.: Deutsch Archiv. f. klin. Med., XXXIV No. 4. P. 443, 1883.

[6]Cushing, Harvey: Pituitary Body and its Disorders, 1912, Philadelphia and Shattuck Lecture, Boston Med. and Surg. Journal, 1913 P. 168, 901.

[7]Kary, Clara: Virchow's Arch. f. path. Anat., 1924, P. 252-734.

[8]Elmer, A. W., Kedzierski, J. and Scheps: Wien. klin. Woch., Vol. 41 P. 591, 1928.

[9]Brugsch, T., Dresel, K. and Lewy, F. H.: Ztschr. f. exper. Path. u. Therap., Vol. 21 No. 2, 1920 and Ztschr, f. d. ges. exper. Med., Vol. 25, No. 262, 1921.

[10]Harris, Seale: Hyperinsulinism and Dysinsulinism, J. A. M. A., 93:729. Sept. 6, 1924.

[11]Wilder, R. M.: Allan, F. N.: Power, M. H. and Robertson, H. E.: Carcinoma of the Islands of the Pancreas: Hyperinsulinism and Hypoglycemia, J. A. M. A., 89:348, July 30, 1927.

[12]Leschke, Erich: Zeit. klin. Med., Vol., 108, 1928.

[13]Pick, E. P.: Verhand. d. Gesellsch. f. Verdauungs u. Stoffwechs., Vol. 6, P. 125, 1927.

[14]Elwyn, H.: Edema and its Treatment: Macmillan, 1929.

[15]Hiller, F. and Tannenbaum, A.: Archiv. of Neur. and Psych., Vol. 22, P. 901 to 907, November, 1929.

[16]Hiller, F. and Grinker, R. R.: Arch. of Neur. and Psych., Vol. 22, P. 919 to 925, November, 1929.

[17]Von Noorden, C. and Isaac, C.: Die Zuckerkrankheit und Ihre Behandlung, Berlin, Verlag von Julius Springer, 1927.

[18]Umber, F.: Ernährungs u. Stoffwechsel krankheiten, Berlin, P. 202, 1928.

Obesity

Observations on Treatment by Dietary Measures

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THE excessive deposition of fat in the body, either as a result of overnutrition, or a disturbance of the glands of internal secretion, is quite a common occurrence clinically. Obesity may be divided etiologically into two types, not always clearly defined—the exogenous and endogenous varieties. In the exogenous group are included those cases in which the only discoverable cause may be attributed to race, heritage or habits of life. The tendency toward a gradual increase in the general deposition of fat during and after middle life, is largely dependent on changes in habits. Over indulgence and ignorance as to the need of curbing the appetite, with the associated decrease in physical activity, and lessened energy requirement, is a contributing factor in the development of obesity. Exercise is likely to be reduced, and material success, with its associated abundance of good food, favors fat storage in the body. Especially is this true in the male of the species. Corpulency in women is much more common, and apparently less influenced by habits. The periodicity of sex function in women, seems to have a greater influence on fat deposition than is the case in men. After the climacteric, there is commonly a marked tendency to corpulency. Opposed to these general tendencies, are those individuals who retain a constant weight within wide limits of food ingestion.

Newburgh and Johnston insist that obesity is always caused by an overabundant inflow of energy. The excess is deposited as adipose tissue. Body weight is the resultant of two factors; either a gain or loss of tissue, or a gain or loss of water. The loss of one and a gain in the other may neutralize each other; or a large retention of water may cause a gain in weight, even though body tissue has been consumed, and may lead one to draw erroneous conclusions, if there is a failure to take water exchange into consideration. The response of various types of obese people, does not differ from that of normal people. All of them oxidize body tissue in accord with the prediction from the caloric deficit. Retention of water may proceed for several days, or loss of water may be suddenly precipitated.

Wm. E. Preble in an analysis of one thousand cases, came to the conclusion that obesity is almost invariably due to bad dietary habits, and not to hereditary errors in metabolism. Strouse and others have found, that there is a constitutional tendency to obesity. While the food intake may not be great, the tendency to obesity is great. The basal

metabolism in the obese is usually within normal limits. Their interesting contribution is that the specific dynamic effect of proteins is much less in the obese than in the thin individuals. The same is true for carbohydrates. They also found that during a state of fatigue, in the normal individual the heat production is slightly increased, and the mechanical efficiency is lessened. When obese individuals are compared with normals, the heat production is much greater, and the mechanical efficiency is much less; also, fatigue came sooner in the obese, than in the undernourished.

B. D. Bowen has shown that the vital capacity in obese and overweight individuals is but slightly less than normal. The tendency to dyspnea in the obese may be accounted for, in part at least, by a reduction in vital capacity. The weight of obese subjects should be reduced slowly, especially if there is dyspnea, as a definite reduction in vital capacity occurs with the development of symptoms of a cardiac nature.

Hagedorn and others have found that the respiratory quotients in obese persons are lower than in normal individuals. Their results confirm the hypothesis that obesity is due to a qualitative anomaly in metabolism, i. e. an abnormal increased transformation of carbohydrates into fat. It has been shown that a relation exists between the percentage overweight and the respiratory quotient in obese subjects. Patients with great overweight have a particularly low respiratory quotient, while those with less overweight, have a respiratory quotient which is nearer or within the normal zone.

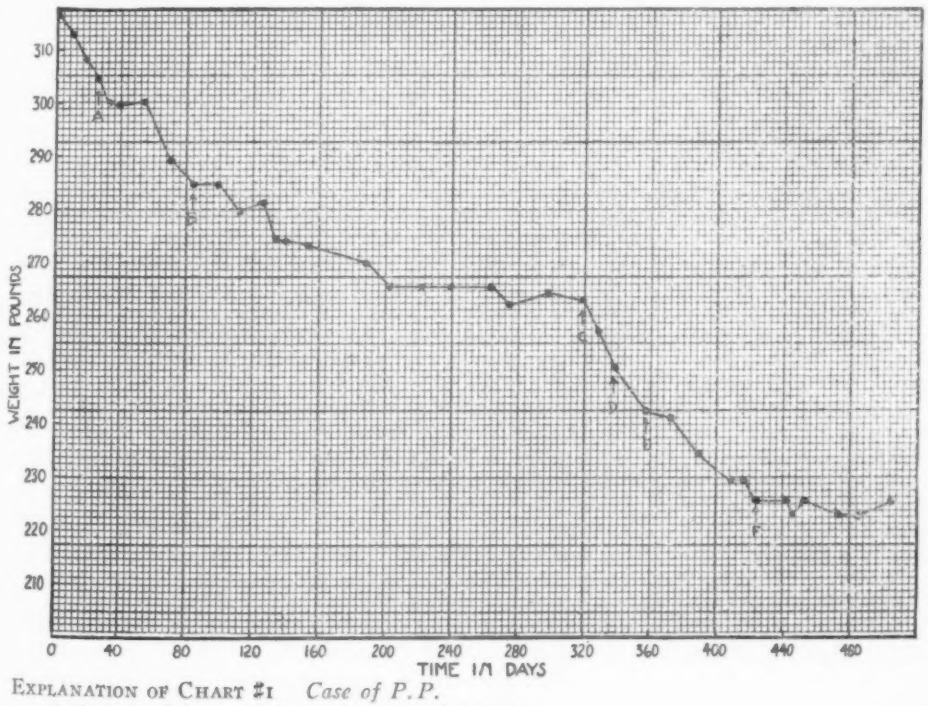
Goldblatt, in his study of sixty cases of exogenous obesity, found, that there is no impairment in the oxidation of carbohydrates, but a delayed storage. This reduction in the storage power was considered to be secondary to the obese condition. No abnormalities of carbohydrate metabolism were discovered in one hundred adolescents with endogenous obesity.

The endogenous or constitutional group of obesities comprises those cases in which there is more or less well-defined pathological etiology. From the glands of internal secretion, may be sought the cause of a certain number of these obesities. Castration in either sex is followed by an increase in weight and frequently associated with marked obesity. The tendency to stoutness, subsequent to the menopause, may be included in this category. Tumor of, or in the neighborhood of, the pituitary gland, may lead to extraordinary degrees of adiposity, associated with sexual infantilism. (Fröhlich's Syndrome). This condition is found most frequently in children and young adults. Removal of the posterior lobe of the pituitary gland is followed by a great increase in weight, due principally to the general deposition of fat. Perverted functional activity of the pituitary gland, usually spoken of as hypopituitarism, or hypohypophysismus. (dystrophia adiposogenitalis) may be another cause. Abnormal function of the thyroid, or hypothyroidism, with or without the symptom complex, known as myxedema, may be responsible for large increases in adipose tissue, and the term thyrogenic obesity applied. Any lessening in the basal metabolic rate for

any reason, favors the development of obesity.

Basal metabolism in the endogenous cases has been found to be low, varying from 25% to 50% below normal. In these instances there is no evidence that the fat metabolism is abnormal, but merely that metabolism is less intense. The body requirement is less. Associated with the obesities, due to derangements in the functions of the glands of internal secretion, there are frequently subnormal temperature and a low nervous tension; factors which influence the amount of heat produced. Combined with a low energy requirement, the sluggish habits so commonly found in these cases, and a liberal food intake, the resultant fat increase in the body is a perfectly normal process. Associated with this there is a disturbance of water and salt balance in addition to faulty metabolism.

The general impression that in exogenous obesity the basal metabolic rate is normal, receives additional confirmation in a study made by Topper and Mulier on 35 boys and 35 girls, between the ages of 6 to 14 years, using the Pirquet Standards.



EXPLANATION OF CHART #1 *Case of P. P.*

Patient's weight at beginning was 316½ pounds.

At point A, began the use of moderate doses (6 grains daily) dried thyroid gland substance. Point B. Thyroid therapy stopped, because of reaction, and diet alone continued. At C, again started on thyroid therapy. At D thyroid was reduced to four grains a day, because of slight complaint of nervousness. At E thyroid dosage again increased to nine grains a day, with weekly injections of Aolan. At F, Thyroid and Aolan stopped, and continued on diet alone.

Recht found that obese individuals absorb saline more rapidly than normal individuals. There were, however, marked regional differences, which were not altered by copious drinking of water, or the administration of pituitrin. The administration of pituitrin revealed the existence of a marked antidiuretic action in some cases of obesity. In contrast to this Hunt found in his cases that the limitation of diet, in the so-called constitutional obese, was of no avail, and that subcutaneous injections of 1 cc. of pituitary preparations for two weeks, were useless.

In an attempt to determine just what may be accomplished with the average obese patient that one meets in an outpatient clinic, or in general practice, and what improvement occurs in their general condition, upon a reduction in their weight, this study was undertaken. Those of us who are connected with an outpatient clinic of a large hospital, are constantly impressed by the association of overweight with definite physical complaints on part of the patient. The series of cases studied were not selected because of any special factor in their obesity, but represent patients who came to the medical clinic of the University Hospital for various other complaints. None of them was sufficiently disturbed by their overweight to mention it as their chief complaint. The cases analyzed are those which came under our observation within a definite period of time.

In beginning our dietary management, we realized that the underlying principles of all reduction were the maintenance of nitrogen equilibrium, and at the same time keeping the carbohydrate and fat ingestion at such a level that the total food intake is below the daily requirement, with the consequent result that body fat is called upon to make up the deficiency. We desired to establish a gradual loss of weight, and in this way maintain a sense of well being on the part of the patient, with a greater likelihood of continued adherence to diet.

A well balanced diet is essential for a low caloric intake. Such a diet must provide a variety of food, which will furnish in abundance the protein needed for muscle building and repair, the necessary fuel needed for energy, and regulating food containing vitamins and minerals, which influence all body processes and increases resistance to disease.

A reducing diet should be planned on the total fuel value of the diet for a normal individual, being based on the average height, weight, age, sex and occupation.

We realized that any plan of dietary restriction instituted was not under strict control as to dietary adherence.

In order to be assured that the factor of error in our observations should be minimized, we did not follow the plan of Grafe, by restricting the caloric intake in proportion to the excessive weight of the patient. For the same reason, we did not make any effort to control the salt intake. Knowing the average run of patients seen in a medical clinic, the dietary management advocated by Evans and Strong would be subject to criticism, as there is an ever present possibility of the patients studied, adding snacks to their diet, which, to them, appears to be of little importance, but appreciably increases their caloric intake.

By a more liberal caloric diet, we felt that greater adherence to their regime was possible, and better cooperation on part of the patient. One could also figure their caloric intake as being more accurate.

All the patients were placed on a diet of approximately 1400 calories, as such a diet will allow a gradual loss of weight. The protein was calculated to be about 1.3 gm. per kilo of body weight. This insured the patients against using their own protein, consequently little or no weakness was felt during the period of dieting. The carbohydrate approximated 200 grams, and with this amount danger of acidosis was lessened. A sufficient quantity of carbohydrate was given in the form of 5% and 10% vegetables to satisfy the patients' appetite. No free fat was given. The amount of fat in the diet was combined with the food in the form of egg, cheese, meat, etc. In addition sufficient vitamins and minerals were provided to prevent any possibility of malnutrition developing.

With this diet, weight was not lost too rapidly, nor did it interfere with the patient's routine of life.

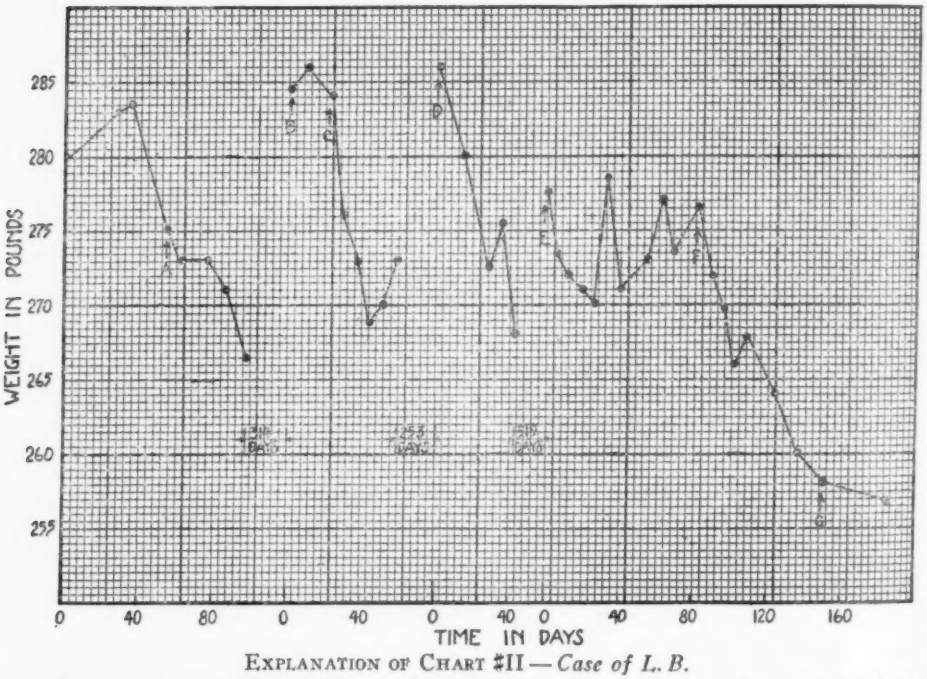
The cases were instructed to report weekly for observation, and at each visit a check-up on their diet was made by the dietitian. In spite of this we found it difficult, in all the cases, to maintain a strict adherence to the diet, over a long period of time. Allowing for occasional lapses, we felt that those patients in whom definite weight loss occurred, had adhered closely to their outlined regime. In those patients in whom we failed to obtain any evidences of weight loss, after several weeks, we obtained a confession from them that they had lapsed in following their instructions. Often in such instances, following a lecture on the importance of cooperation on their part, there occurred a subsequent loss in weight. No attempt was made to advise exercise, because of the difficulty in standardizing and checking such measures.

As all our cases were women in whom there was not much likelihood of a change in their general routine and habits of life, we can safely assume that the question of physical activity was not an important factor in their reduction of weight.

The total number of cases studied was fourteen, and they were kept under observation for a period varying from three to eighteen months. One of these cases showed a definite evidence of glandular disturbance — a thyropituitary type, with a basal metabolism of -12,—and this case we did not include in our study. We confined ourselves to those obese individuals, who, as far as we could determine, came under the exogenous classification. The basal metabolism in all these cases were within normal limits. The highest was +18 and the lowest +5.1. They were all women who were married, and gave a history of having one or more childen. Their ages varied. One case was 25 years old; five were between 30 and 40 years; six were between 40 and 50 years, and two were 54 years. One of the patients had definitely passed her climacteric, while in another in whom we succeeded in obtaining a marked reduction in weight, there occurred a return of her menstrual flow, after a lapse of two years. Two of the cases, who, at the be-

ginning of our study, were going through the climacteric, during the period of observation, had a normal restoration of their menstrual flow.

As a group, their chief complaints were mainly those of back pains, joint symptoms, dyspnea on exertion, gastric distress and nervousness. In one of our cases there was a definite history of gall bladder disease, and in two others the physical findings were indicative of myocardial involvement. One case, the only complaint was that of a Taenia saginata infestation, and upon cure of this condition the patient failed to return for further observation. One of the cases, with definite myocardial disease, was referred to us from the eye clinic because of an optic neuritis; and coincident with her re-



EXPLANATION OF CHART #II — *Case of L. B.*

First curve represents patient on diet alone. A primary increase in weight noticed, instead of a decrease. Following a lecture to the patient, with insistence upon strict adherence to the diet, there is a marked drop. At A, Thyroid in moderate doses was given, with continued loss in weight.

B represents the weight of the same patient after a lapse of 314 days, with no dietary regime. Again placed on a diet. At C, Thyroid started in conjunction with the diet. D represents weight of same patient after a lapse of 253 days. This time immediately placed on diet, plus thyroid therapy. At E, patient returned after a lapse of 519 days. At this time we had undertaken a detailed study of our obese patients; hence we lectured her on the desirability of co-operating with us, and continuing under our constant observation. She was placed on diet, plus thyroid, with periods in which diet alone was used. The increased loss of weight occurred at time of thyroid therapy. At point F, after a period of diet alone, patient was placed on increased thyroid dosage (nine grains daily) with weekly injections of Aolan. At G Thyroid and Aolan discontinued.

duction in weight, there occurred a disappearance of her optic neuritis. There was also one case which presented definite evidence of focal infection, with tonsils that were diseased and from which pus could be expressed, and in this instance, reduction in weight failed to bring about any improvement in symptoms.

An interesting observation noted was the effect upon the blood pressure readings following a definite reduction in weight. The blood pressure readings in this series ranged as follows: In 10 cases it varied between 110 and 150 m.m.Hg. Between 175 and 200 in three cases, and above 200 in one case. In the one patient whose blood pressure was above 200 at the beginning of our study, we were able to show a reduction of 60 mm. Hg. In the three cases which were between 175 and 200, we obtained an average reduction of 40 mm. Hg.

In a paper published by Masters and Oppenheimer, subsequent to our study, they clearly demonstrated the general improvement in symptoms evinced by obese cases, especially in circulatory and cardiac cases. They found a drop in blood pressure, reduction in pulse rate, and general improvement in cardiac function, shown by roentgenogram and electrocardiogram; also a distinct increase in the patient's exercise tolerance, with the reduction in weight.

In the dietary management of our cases, we failed to obtain any loss of weight in three patients, because of lack of co-operation on their part, and the results obtained were negative in character. Four were kept on diet alone, and by this measure alone, we were able to maintain an average loss of weight, varying from one to three pounds per week, depending upon degree of co-operation. Two cases, in whom there was observed a desire to co-operate, were placed on mild doses of dried thyroid gland substance, averaging six grains a day and there was noticed an additional loss of weight of approximately a pound a week. In five cases we kept the patient on a diet, and because we reached an impasse in their weight loss, we placed them on thyroid therapy, and found that the average period before one could expect a reaction to the thyroid therapy varied from four to six weeks. After that time they began to complain of nervousness and cardiac palpitation. In these cases we then started them on weekly injection of 5 cc. of aolan, in accordance with the findings of Julius Bauer of Vienna, who observed that he could continue the use of thyroid for a much longer period without reaction occurring, by the coincident use of a non-specific foreign protein. In our five cases we also found that thyroid therapy could be continued, after thyroid reactions were observed, for an extra period of time, varying from five to eight weeks. In two of these cases we increased the daily dosage of thyroid from six to nine grains per day, and we were consequently able to obtain a greater reduction in weight and thyroid symptoms did not develop until after a month of active treatment. Our criterion of thyroid reaction was objective evidence, such as rapid pulse or tremors, or subjective complaints on part of the patient, such as nervousness or cardiac palpitation.

In the cases studied, where dietary measures were successful, there occurred a definite loss of weight in ten of the cases. The aggregate loss was 385 pounds. The shortest period of observation was three months in one case, with a loss of eleven pounds, and the greatest single loss was 93½ pounds in a period of sixteen months.

Conclusions

1. In cases of obesity, an adherence to a prescribed diet, as outlined, will bring about an amelioration in symptoms, a definte lowering of blood pressure, when it is high, and a general improvement in the patient's physical condition.

2. Average loss of weight depends upon length of observation, and degree of continued adherence to a diet.

3. Strict adherence to a balanced diet will bring a gradual loss of weight, varying from one to three pounds per week, up to a certain point, depending upon degree of co-operation on part of the patient.

4. Moderate doses of thyroid therapy, plus diet, will cause an extra loss of weight, averaging one pound a week, and one can usually continue thyroid therapy from four to six weeks before evidence of thyroid reaction occurs.

5. The moderate use of thyroid therapy, without adherence to a diet, fails to cause an appreciable loss of weight.

6. Aolan injections, plus thyroid therapy, give one an opportunity for greater dosage of thyroid, with an increased loss of weight, and a prolongation of the period of time before reaction occurs.

7. In patients where an adherence to a diet is difficult to maintain, a course of thyroid therapy, with weekly injections of 5 c.c. of aolan, will help to bring a reduction of weight sufficient to encourage the patient. This will prove beneficial in bringing about further dietary adherence.

BIBLIOGRAPHY

Newburgh, L. H. & Johnston, Margaret W.: Endogenous Obesity. J. Am. Dietet. A., 5:275-1930.

Preble, W. E.: Obesity, Observations in 1000 cases. Boston Med. & Surg. Journal, 188:617. 1923.

Strouse, S. & Dye, M.: The Relation between Food Intake and Body Weight in Some Obese Persons. Arch. Int. Med., 34:267, 1924.

Wang, C. C. & Strouse, S & Saunders, A. D.: Studies on the Metabolism of Obesity. The Specific Dynamic Effects of Various Foods. Arch. Int. Med., 34:573, 1924.

Hagedorn, H. C., Holten, C., Johansen, A. H.: Arch. Int. Med., July 15, 1927.

Wang, C. C. & Strouse, S.: Metabolism of Obesity. Archives Int. Med., 36:293, 1925.

Bauman, L.: Obesity, Recent Reports in the Literature and Results of Treatment. J. A. M. A., 90:22, 1927.

Wang, C. C., Strouse, S. & Smith, E. A.: Influence of Fatigue on the Heat Production, During Muscular Work in Obese, Normal and Thin Subjects. J. Biol. Chemistry., 75:28, 1927.

Bowen, B. D.: The Relation of Age, and Obesity to Vital Capacity. Archives Int. Med., 31:579, 1922.

Brown, G. E. & Keith, N. M.: Blood and Plasma Volume in Obesity. Arch. Int. Med., 33:217, 1924.

Terry, A. H., Jr.: Obesity and Hypertension. J. A. M. A., 81:1283, 1923.

Topper, A. & Mulier, H.: Basal Metabolism of Children of Abnormal Body Weight. J. A. M. A., 92:1903-1929.

Recht, G.: Water Content of the Skin in Obesity. Klin. Wchnschr., 8:1748, 1928.

Hunt, T. C.: Treatment of Constitutional Obesity with Hypophyseal Preparations. Klin. Wchnschr., 211:1682, 1928.

Bauer, Julius: Ueber Fettsucht. Wiener Klin. Wchnschr., 9:1926.

Goldblatt, M. W. *et al.*: A Clinical & Metabolic Study of Obesity. Quart. J. Med., 21:325, 1928.

Evans, F. A. & Strang, J. M.: Departure from Usual Methods in Treating Obesity. Am. J. M. Sc., 177:339, 1929.

Masters, A. M. & Oppenheimer, E. T.: J. A. M.A., 1652, 1929.

Grafe, E.: Theory & Practice of Reducing Treatment. Medizinischer Klinik, 25:373, 1929.

Chlorotic Anemia with Achlorhydria, Splenomegaly, and Small Corpuscular Diameters*

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THE brilliant specific results of liver therapy in pernicious anemia announced by Minot and Murphy[4], following upon the demonstration by Whipple and Robscheit-Robbins[8] of the importance of liver feeding in the chronic anemias of dogs, induced by repeated bleeding, have led to a widespread attempt to treat all anemias with liver. In many of the so-called secondary anemias the response to liver therapy is only partially successful and in others entirely disappointing, when compared with the results in pernicious anemia.

It is the object of this paper to present the clinical features of a group of anemic patients, all of whom failed to derive benefit from liver therapy, all of whom responded as promptly and specifically to massive doses of iron as pernicious anemia responds to liver. From the standpoint of hematological criteria the anemia here described is differentiated from pernicious anemia by its low color index, red corpuscles the average size of which is below normal, without bilirubinemia; which is in sharp contrast to the high color index, macrocytosis, and bilirubinemia of the latter. It shares achlorhydria as a common characteristic with pernicious anemia, and, like the latter, has a tendency to recur.

In 1913 Knud Faber called attention to the association of achylia gastrica with simple anemias of chlorotic type as well as with pernicious anemia. In 1924 he published with H. C. Gram[1] further observations. Of 63 patients with uncomplicated achylia, 36.5 per cent were anemic. In the patients with normal hemoglobin the color index fluctuated about 1, while the index in the anemic cases was nearly always decreased. In the more pronounced cases the small size of red corpuscles was clearly visible in the stained films. The anemia was distinctly more frequent in women than in men and most of the severe cases occurred among the former. Megalocytes and megaloblasts were never observed. Stippling and reticulation were observed only during treatment with large doses of iron and never in untreated cases. The leucocytes were either normal in number of slightly low. Faber and Gram did not give detailed case reports of the clinical features of this achylic chloranemia. They state that it is of a

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rather benign character, not lethal, but refractory toward treatment, and that it tends to recur. It occurs in both sexes and at all ages. No tendency to spontaneous or permanent recovery was noticed. The most successful treatment was with massive doses of iron.

More recently, Kaznelson, Reimann and Weiner[3] have given detailed case reports of patients with an "achylic chloranemia." Their patients presented themselves with a variety of complaints, chiefly those due to the anemia, such as palpitation, weakness and pallor, though many patients came under observation because of gastro-intestinal symptoms, such as diarrhea associated with achylia. Their patients were of all ages and of both sexes. Females predominated slightly. Among their patients splenomegaly was not a frequent finding. Some of their patients had a Hunterian glossitis, and papillary atrophy, and some had paresthesias suggestive of a disorder of the posterior columns of the spinal cord. Some patients had a koilonychia of both hands and feet. The blood changes were described as follows: anemia with low color index, without leucocytosis, sometimes with a slight lymphocytosis and normal platelets. The serum was colorless and showed no increase in bilirubin, or other evidences of heightened blood destruction. Urobilinogen was found in the urine only in traces. Evidence of occult bleeding was absent. As to therapy, these authors found that liver was wholly inactive, and they regarded iron as a specific for achylic chloranemias.

An important finding is reported by Weiner and Kaznelson[8], who studied the marrow obtained by sternal puncture, before and after treatment. They found an excessive increase in erythroblasts, which in all cases were exclusively normoblasts, 30-47 per cent of the marrow cells as compared with the normal 20 per cent. Megaloblasts were never found. Two punctures of the sternum following successful treatment revealed normoblasts in normal proportions.

The discrepancy between the chronic anemia and the richness of the bone marrow in erythroblasts, without evidences of increased hemolysis or blood loss, was very striking. The inference was drawn that there was a disturbance in the maturation of the erythroblasts in the bone marrow. After administration of iron they noted a rapid increase in erythrocytes taking vital stains (reticulocytes).

Most descriptions of true chlorosis mention small diameter of red cells as a matter of diagnostic importance. Minot[5] states that "with improvement, increase in the number of red cells, often to normal or above, occurs long before the cells regain their size or proper complement of hemoglobin."

In connection with the cases to be reported here we chose the method of Price-Jones[7], to secure data upon the average diameters of the red corpuscles in chlorotic anemias. The frequency of distribution of corpuscular diameters was determined by measurement of 300 corpuscles in freshly dried smears, fixed and stained with Wright's stain, using an ocular micrometer. The results obtained were subjected to analysis according to the recommendations of Pearl[6] to determine the significance of the differences in mean diameters

found in relationship to the probable errors of the means.

The ocular micrometer disc was ruled to 5 mm. in 0.05 mm. divisions, with every twentieth line numbered. With an oil immersion lens (97x), a number 10 ocular and a tube length of 160 mm., each line measured 0.869 μ. Cells falling on the ruled space were measured as 4.0, 4.5, 5.0, 5.5, etc., lines in diameter. Measurements were made on smears taken as nearly as possible under the same conditions and at the same time of day in each case. Hemoglobin was determined in a hemoglobinometer of the Sahli type with a permanent glass standard. Each diluting tube was calibrated with a standard hematin solution made from blood whose oxygen capacity was accurately determined by the method of Van Slyke and Neill[12]. Forty minutes were allowed for the development of the color of acid hematin. Red cell counts were made with certified counting chamber and pipettes. The color indices were calculated on the basis of a correspondence of 5 million corpuscles and 100 per cent hemoglobin equal to 15.0 grams per 100 cc. of blood.

Case Reports

Case I. No. 3771. A married woman 35 years old was first seen November 4, 1926, for the complaint of perpetual fatigue and pallor. These symptoms dated from early childhood. Anemia became marked and was accompanied by a nervous breakdown while she was in college. She married at 26 and gave birth to three normal children in 9 years. In each pregnancy she was quite anemic. After the last pregnancy in the spring of 1925 her hemoglobin was 45 per cent. Aside from the exacerbations of fatigue and pallor there were unusually few specific illnesses. There had been no unusual blood loss, no peculiar pigmentation or jaundice. The catamenia began at 13 years and was quite normal. The pregnancies were marked by rather prolonged vomiting and by pressure symptoms. The first two labors were induced after term but were otherwise not unusual.

The *examination* revealed a normally developed and well nourished woman, with marked pallor, no jaundice, nor abnormal pigmentation. There was no general or regional enlargement of lymph nodes and no evidence of purpura. The tongue revealed no papillary atrophy. There was a soft systolic murmur heard over the apex of the heart, which was otherwise normal. The spleen was *palpable* just below the costal margin. The liver edge could be felt 2 cm. below the costal margin in the mid-clavicular line. The blood pressure was 124 mm. of Hg. systolic, 78 diastolic. There was a moderate endocervicitis, but no other pelvic abnormality. The neurological examination was normal throughout. Vibration was well perceived. The urine was normal on several examinations and the phenolsulphonephthalein test of renal function showed normal dye excretion.

The blood Wassermann test gave a weak positive reaction with the cholesterinized antigen and the Kahn precipitation test was ++.

Two gastric analyses were done, which showed *an absence of free hydrochloric acid* in the fasting contents and after an Ewald meal, with very low total acidity.

The peculiar feature of the blood examination was an *anemia with a low color index.*

On November 4, 1926, the blood examination was as follows: hemoglobin 58 per cent (100% = 15 gms. Hgb. per 100 cc.). RBC 4,770,000; WBC. 5,400. The differential count was not unusual. There was considerable anisocytosis and achromia of red cells. Platelets were normal. The patient took liberal amounts of liver in her diet several times a week. On January 11, 1927, the hemoglobin was found to be 70 per cent, RBC. 4,700,000; WBC. 6,050. The smear revealed a differential count as follows: polymorphoneutrophiles 67%, eosinophiles 2%, monocytes 5%, lymphocytes 34%, unclassified 2%. These latter were mononuclear cells with large nuclei, and scattered cytoplasmic gran-

ules which were not azurophilic. Platelets appeared to be reduced in number.

An attempt was made to improve the anemia by diet from January, 1927, to October 15, 1928. She took liver three times a week throughout this period. On February 23, 1928, the patient suffered from an attack of facial erysipelas lasting for five days. On discharge the blood count, February 27, 1928, was as follows: hemoglobin 58 per cent, RBC. 4,250,000; WBC. 7,200.

On October 19, 1928, the color index was still found to be low, so that it was decided to try the effects of massive doses of Blaud's pills, of which 12 were taken daily for 30 days. This is equal to 10.44 gms. of iron.

The successive blood counts were as follows:

Date 1928	Hemoglobin per cent	RBC x 10^6	Color Index
Oct. 19	57	5.25	0.54
Oct. 29	65	5.06	0.64
Nov. 14	78	5.00	0.78
Nov. 17	85	5.52	0.77
1929			
Feb. 9	81	4.51	0.89
Apr. 4	82	4.86	0.84

The patient remarked that her feeling of perpetual fatigue was relieved for the first time in her memory since early childhood. The spleen was no longer palpable. She has retained excellent health by occasional resort to iron administration.

Case No. II C.F., No. 3950. A young married woman, aged 35 years, was admitted to the hospital on July 15, 1929, complaining of painful swollen joints, anemia, and weakness. The arthritis, first noted two years before, had involved first the hands, and later many other joints. The course of the arthritis was one of exacerbations and remissions, during which the joints did not return to normal. Each exacerbation left the joints involved more disabled, more swollen and deformed. A marked exacerbation followed the birth of her fourth and last child, six months before admission. This attack was febrile and she recalled having night sweats. Each of her five pregnancies had been associated with marked ill health. The first terminated by miscarriage. The remaining four gave birth to children, now aged 11, 8, and 6 years and 6 months. The last four pregnancies and labors were normal, except that each left her so "run down" that it required many months for recovery. There was no history of abnormal blood loss, no jaundice, nor purpura. The catamenia had been normal in every way, except that menstruation had not been re-established since the birth of the last child. The past history revealed nothing of significance not included in the foregoing resumé. One sister suffered from a similar illness.

Physical examination revealed a small moderately emaciated woman, with brownish skin, but bluish white sclerae, and extremely pale mucous membranes. There was no evidence of purpura, or edema, or general enlargement of lymph nodes. There was an obvious deforming arthritis of the hands, with some muscular atrophy, spindle shaped joints with thin atrophic skin covering periarticular swellings, not acutely tender but somewhat limited in motion and showing malalignment of phalanges.

TABLE 1. SUMMARY OF DATA OF CASE I.

Date	Hgb. %	RBC 10^{x6}	Color Index	Lower Size	Upper Size	Spread	Apex	Mean*	Median	Standard Deviation
10-19-'28	57	5.25	0.54	4.345	8.255	3.910	6.083	6.3032	6.0358	0.7005
4 -4-'29	82	4.86	0.84	5.214	9.559	4.345	6.952	7.2851	7.0079	0.8247
7-15-'29	85	4.67	0.90	5.214	9.124	3.910	7.386	7.2315	7.0769	0.6278
11- 7-'29	81	4.68	0.86	6.083	8.690	2.607	6.952	7.3633	7.0857	0.5334

*The difference between means 1 and 4, divided by the square root of the sum of the squares the probable errors of means 1 and 4, gives a quotient of 18.87, which shows that the difference is significant statistically.

Only positive findings of the regional examination are given: Most of the teeth had been extracted, the few remaining in the lower jaw showed marked pyorrhea. The tongue seemed rather smooth on its edges. The tonsils were small, but the faucial pillars were somewhat red and injected. No abnormality of the lungs or heart was found, except a soft apical systolic murmur which was not transmitted beyond the precordium. The spleen was palpable 5 cm. below the costal margin, presenting a typical notch and a hard smooth surface. The liver and kidneys were not palpably enlarged. There was diastasis of the rectus muscles but no ascites. The cervix uteri was deeply scarred. The neurological examination revealed sluggish knee jerks. The ankle jerk could not be elicited. Postural and vibratory sensations were normally perceived.

The blood counts were as follows: hemoglobin 40 per cent (6 gm. hemoglobin per 100 cc.); R.B.C. 3,950,000; W.B.C. 3,320. The differential count showed polymorphoneutrophiles 63 per cent, lymphocytes 26 per cent, eosinophiles 1 per cent, basophiles 2 per cent, monocytes 6 per cent, and neutrophile metamyelocytes 2 per cent. The red corpuscles showed considerable anisocytosis and achromia with little poikilocytosis. The icterus index of the blood plasma was normal. A fragility test with hypotonic salt solution showed hemolysis beginning at 0.46 per cent, and complete at 0.36 per cent NaCl. The Wassermann and Kahn tests on the blood were negative. The urine contained a trace of albumin but no sugar, urobilin, or blood. A few hyaline casts were seen. The gastric analysis revealed *no free hydrochloric acid* in the fasting contents, or after a test meal of 7 per cent ethyl alcohol. A roentgenogram of the hands revealed atrophic changes in the epiphyses and of the small bones of the wrist. One of the chest revealed no abnormality of the heart. The markings at the root of the lung were somewhat increased in density.

The treatment of this patient was partly directed toward the arthritis and partly toward the anemia. For the former she was given neocinchophen and intravenous injections of amiodoxyl benzoate. The treatment of the anemia consisted, at first, of addition to the diet of two vials daily of a liver extract known as "secondary anemia" extract, (15), differing from the one commonly known as the Minot-Cohn extract No. 343. The diet was a mixed diet known as "House Diet" in the hospital. This diet varies greatly from day to day. It furnishes about 80 gm. protein, 2500 calories and 8-15 mgm. iron. (Estimated). Twenty-four vials of the liver extract were given between July 17th and 29th. The blood counts at the beginning and end of this period were as follows: July 17th: Hgb. 40 per cent, R.B.C. 3,950,000, W.B.C. 3,320, on July 29th: Hgb. 45 per cent, R.B.C. 4,000,000, W.B.C. 4,000. During this period in which five blood counts were made, the reticulocytes were always less than 1 per cent. In the amounts given the "secondary anemia" liver extract (15) produced no demonstrable effects. It was discontinued.

On July 30, 1929, the patient was given mass of ferrous carbonate 1.0 gm. four times daily for 30 days, making a total of 120 gm. equivalent to 42 gm. ferrous carbonate. Marked improvement occurred as is shown by the following blood counts:

Date 1929	Hgb. per cent	R.B.C. x 10^6	Reticulocytes
July 29	45	4.00	less than 1%
Aug. 2	50	4.00	
Aug. 7	60	4.12	2%
Aug. 8			3%
Aug. 12	70	4.88	1%
Aug. 17	72	5.05	
Aug. 23	70	4.55	
Aug. 30	85	4.85	

The spleen was somewhat reduced in size but still palpable at the costal margin. Subjectively the patient felt better and was discharged from the hospital much improved. Administration of iron was not continued. Six weeks later, Sept. 16, 1929, her blood count was: Hgb. 84 per cent, R.B.C. 3,960,000.

Again she was given mass of ferrous carbonate gm. 2.0 daily. When seen October 25, 1929, the blood count was as follows: Hgb. 84 per cent, R.B.C. 4,740,000. At this time her appearance was much improved but she still suffered from her arthritis.

TABLE 2. SUMMARY OF DATA IN CASE II.

Date	Hgb. %	RBC 10^{xe}	Color Index	Lower Size	Upper	Spread	Apex	Mean*	Median	Standard Deviation
7-15-'29	45	3.91	0.56	4.779	9.124	4.345	6.083	6.4507	6.1686	0.7007
7-20-'29	40	3.05	0.65	5.214	9.559	4.345	6.952	6.9172	6.666	0.7396
10-11-'29	84	3.93	1.06	5.214	8.690	3.476	7.821	7.3488	7.1456	0.5823
10-28-'29	84	4.74	0.88	5.648	9.559	3.911	7.821	7.5062	7.2779	0.5973

*The difference between means 1 and 4, divided by the square root of the sum of the squares of their probable errors is 19.85, which is statistically significant.

Case 3. C. O. No. 3213. A young woman aged 19 years, unmarried, was admitted to the hospital Oct. 4, 1926, complaining of a "gnawing feeling in stomach" before meals, gaseous "indigestion" with belching and pyrosis, and occasional attacks of vomiting. This condition had been complained of for at least 8 years. The appetite was good. The bowels were habitually constipated. She had never had jaundice, clay colored, tarry or bloody stools.

For five years she was notably pale, and her pallor had been treated by means of a diet of milk and eggs and small doses of iron, without apparent success. Her weight remained stationary between 115 and 120 lbs. The only other symptoms were a perpetual feeling of fatigue, dyspnea on exertion, and, for 8 months preceding admission edema of ankles had been noted.

The past history and review of symptoms yielded little additional information. The patient had measles as a small child, and whooping cough at age of 6 years. The family history had no bearing on patient's condition.

On physical examination the positive findings were as follows: The patient was a well developed, well nourished white girl of 19. Her skin of faint olive tint, smooth and of fine texture, was pale. The mucous membranes were markedly pale. The sclerae were bluish white. The hair was thin. The nasal half of right eyebrow was missing. The pubic hair was of masculine distribution. The voice was deep and rather harsh. No general glandular enlargement was found. There was slight pretibial edema. The regional examination revealed few other abnormalities. There was considerable pulsation in the vessels of the neck. The heart was normal in size, rate and rhythm. A systolic blowing bruit limited to the apical portion of the precordium was heard. The blood pressure was 108 mm. Hg. systolic, 60 diastolic. The abdominal examination was negative except that the tip of the spleen could be felt distinctly on deep inspiration. The pelvic and rectal examination revealed a retroverted uterus. The deep and superficial reflexes were normal. Vibratory sense was well perceived.

The urine was normal on routine examination. The stools contained no blood, ova or parasites. The blood Wassermann reaction was negative. Hgb. 55 per cent (7.25 gm. per 100 cc.). R.B.C. 4,310,000. W.B.C. 6,880. The differential count was not abnormal. The red corpuscles showed slight anisocytosis. Platelets were present in moderate numbers. The cell volume by hematocrit was 38 per cent. The fragility of the red cells to hypotonic salt solution was not abnormal. The van den Bergh test showed no increase in bilirubin in the plasma.

The gastric juice on two examinations contained no free hydrochloric acid in fasting specimens or after an Ewald meal. Spinal puncture yielded a normal fluid, with no increase in number of cells, or protein. Wassermann test and colloidal gold curves of the fluid were normal.

The roentgenologist reported no abnormalities of the gastro-intestinal tract after investigation by a barium meal. The spleen was seen to extend below the costal margin, but did not appear to be very large. A cholecystogram was made subsequently, March 30, 1927, which revealed a normally functioning gall bladder.

A determination of the basal metabolism on March 9, 1927, was reported as -5.8 per cent. (Aub and DuBois standard).

The response of this patient to various

forms of therapy for the anemia is outlined below:

Date	Hgb. 100%=15 gm.	R.B.C. x 10^6	Remarks on Progress and Therapy.
			Given dilute HCl with meals
Oct. 5, 1926	55	4.31	3 Blaud's pills daily.
Dec. 2, 1926	55	4.75	Sodium cacodylate — 2 weeks.
Jan. 14, 1927			Radiation from carbon arc three times weekly
Mar. 29, 1927	55	4.59	to May, 1927.
Apr. 5, 1927			Platelets 340,000. Reiman's method.
Apr. 25, 1927	68		Icterus Index 7.
May 24, 1927	70		Started taking liver, ½ lb. daily.
June 22, 1927	72	5.50	Spleen no longer palpable.
Feb. 7, 1928	70	4.89	Liver diet discontinued. Given 300 Blaud's
June 19, 1928	93		pills. Dose XII pills per diem.
Dec. 19, 1928	90	4.96	Feels well. Able to work.
Feb. 8, 1929	83	4.94	Lost 17 lbs. in weight.

Case 4. J. R. Unit No. 30389. A married woman aged 30 years, was admitted Dec. 7, 1929, and discharged March 3, 1930, to a sanatorium for tuberculosis. The immediate cause of admission was pyuria, which examination revealed to be associated with a pyonephrosis of the left kidney. The history indicated exacerbations and remissions of a urinary tract infection over a period of eight years, starting with an abortion. The infecting organism was B. Coli communis. All attempts to find tubercle bacilli in the urine by smear or guinea pig innoculation failed. During the course of observation in the hospital the patient developed pain in the right side of the chest and abdomen, with signs of atelectasis of the right lower lung, followed by a right pleural effusion. This was aspirated and blood tinged fluid was removed. The cell count of this was as follows: R.B.C. 2,500, W.B.C. 4,500 of which 70% were polymorphonuclears, and 30% were mononuclears. It was sterile on culture and smear, and no tubercle bacilli were found on guinea pig innoculation. A roentgenogram of the chest, made before the onset of the pleurisy, revealed rather heavy shadows at the roots of the lung, and slight evidence of parenchymal tuberculosis under the right clavicle.

On admission it was found that the patient had a marked chlorotic anemia. The hemoglobin was 40 per cent (5.9 gm. per 100 cc.), R.B.C. 4,200,000, W.B.C. 7,000. In common with the other patients in this series she had a persistent *achlorhydria,* and a *palpable* spleen. Under treatment directed mainly toward the relief of her anemia, the infection of the urinary tract improved, and the pleural effusion disappeared. She was transferred for convalescent care to a sanatorium for tuberculosis as a suspect, on account of the pleural effusion, loss of weight of 20 lbs. in seven months preceding admission, and the occasional occurrence of night sweats.

The response of the patient to the various forms of treatment of her anemia is given below:

Date	Hgb. x 10^6	R.B.C.	Remarks on Progress and Therapy
			W.B.C. 7,400. Differential PMN56, Lymph.
Dec. 7, 1929	40	4.24	30 Eosin. 1%, Basoph. 1%, M. & T. 8%,
Dec. 24, 1929	40		myelocytes 4%. Reticulocytes 2.3%. Marked
Dec. 30, 1929			poikilocytosis and anisocytosis. Iron and
Jan. 8, 1930	67	5.25	ammonium citrate 6.0 gm. daily to Dec. 24,
Jan. 18, 1930	73	5.88	1929. Reticulocytes varied 2-4 per cent.
Jan. 22, 1930	78	5.43	Tranfusion 500 cc. citrated blood.
Jan. 25, 1930	81	5.66	Blaud's pills XII daily to Jan. 8th.
Jan. 29, 1930	87	5.57	Vallet's mass of ferrous carbonate 250 gm.,
Feb. 21, 1930	97	5.87	given from Jan. 8th to Feb. 12, 1930.

Case 5. G.D. No. 35672. A married woman 58 years old, was admitted to the hospital May 27, 1930. Complaining of "diarrhea" and "anemia." The onset of her illness was four months before admission, with the passage, three or four times a day, of semiformed stools containing large amounts of mucus. She became very weak and felt her heart pounding. Her physician found that she was anemic. For two months prior to admission she was treated intensively with liver, liver extract No. 343, and "ventriculin," without appreciable benefit. The bowel movements decreased slightly in frequency and occurred without pain or tenesmus. She complained bitterly about vague but horrible abdominal sensations, of borborygmi, and of difficulty in passing flatus. She recalled a similar episode of weakness, anemia, and diarrhea at the age of 30 following childbirth, from which she did not recover for 9 months. After each of her four pregnancies she became anemic and had a recurrence of loose stools. There are many irrelevant details in the history which are omitted here. The patient was in the habit of chewing tea leaves almost incessantly.

Examination revealed a well developed and well nourished woman of 58, who appeared chronically ill. Her skin was dry, rough, inelastic, and of a bronzed color. The mucous membranes and nail beds were very pale. The sclerae were not jaundiced. There was no general glandular enlargement, nor edema. The nails showed a well marked koilonychia. The heart was somewhat enlarged and a soft systolic bruit was audible from the apex to the pulmonary area. The lungs were normal. In the abdomen a markedly enlarged spleen could be felt descending on inspiration from 5 to 8 cm. below left costal margin. There was a rounded mass in the right flank, which was probably the right kidney. The liver edge descended slightly below the costal margin. The tendon reflexes were all normal, as were the plantar and abdominal reflexes. Vibration was well perceived.

The blood count was as follows: Hgb. 37 per cent (5.5 gm. per 100 cc.), R.B.C. 3,660,000. W.B.C. 3,000, with a normal differential count. Reticulocytes 3.7%. The red corpuscles were pale and showed some variation in size and shape. Platelets were normal. The saliva contained 770 leucocytes per cu. mm. so that it was evident that the leucopenia was not of the aplastic type (2). The urine and stools were not abnormal in any way.

The blood sugar, from a fasting level of 90 mg. per cent, rose to 185 mg. in 45 minutes, and was 172 mg. at the end of 2 hours and 15 minutes after the ingestion of 100 grams in glucose. The icterus index was normal, *ie.*, 4. A test of liver function was done by injection of "bromsulphalein." At the end of 5 minutes 15 per cent, and at the end of 30 minutes 10 per cent of the dye remained.

A roentgenological examination of the gastrointestinal tract with a barium meal revealed no local lesion. The stomach showed the indentation of an enlarged spleen. The diagnoses considered were:

(1) Hemochromatosis. The evidence for both cirrhosis and diabetes was insufficient to support this.

(2) Banti's syndrome. Again the evidence for cirrhosis was insufficient.

(3) Achylic chloranemia. The prompt response of the anemia to iron in large doses tends to support this diagnosis, as does the history of earlier episodes of anemia.

The patient was given 12 Blaud's pills, containing 350 milligrams of iron, daily. Of the numerous blood counts made to mark the progress of response to therapy, only six will be recorded here. On each of these six occasions measurements were made of the red cell diameters in fixed blood smears, and these data plotted as Price-Jones curves as shown in Figure I.

A summary of the statistical value of the data, correlating the mean cell diameters with the blood counts and color indices on six occasions, is given in table 3. This summary shows clearly that as hemoglobin and color index rose, in response to treatment with Blaud's pills in large doses, a corresponding increase in mean diameter of red cells occurred, which is six or seven times that which is statistically significant.

Discussion

The five cases described here all have many features in common. The presenting complaints were varied, two were chiefly gastro-intestinal, one of anemia, and two of chronic infections. The third case was one of undoubted chlorosis. The remaining four cases in older women gave indications in the history of probable anemia in childhood or adolescence, though definite data on this point were not available, these patients may represent the recurrence of chlorosis in later life. In all of the histories specific inquiry as to known blood loss, purpura, chronic or recurring jaundice revealed none of these. Four of the five patients had

Table 3. Summary of Data in Case V.

Date 1930	Hgb. %	RBC x 10^6	Color Index	Lower Size	Upper Size	Spread	Apex	Mean*	Median	Standard Deviation
June 1	36	3.80	0.47	4.345	8.690	4.345	6.952	6.684	6.4860	0.6815
3	37	3.66	0.50	3.910	9.559	5.649	7.386	7.0311	6.8301	0.7973
6	52	3.83	0.67	5.214	9.993	4.779	7.821	7.2315	7.0551	0.8290
21	70	4.93	0.71	5.214	8.690	3.476	7.821	7.3502	7.1535	0.6465
28	85	5.49	0.77	5.214	9.124	3.910	7.821	7.5661	7.4170	0.7214
July 5	87	5.31	0.82	5.648	9.993	4.345	7.821	7.7524	7.5675	0.6800

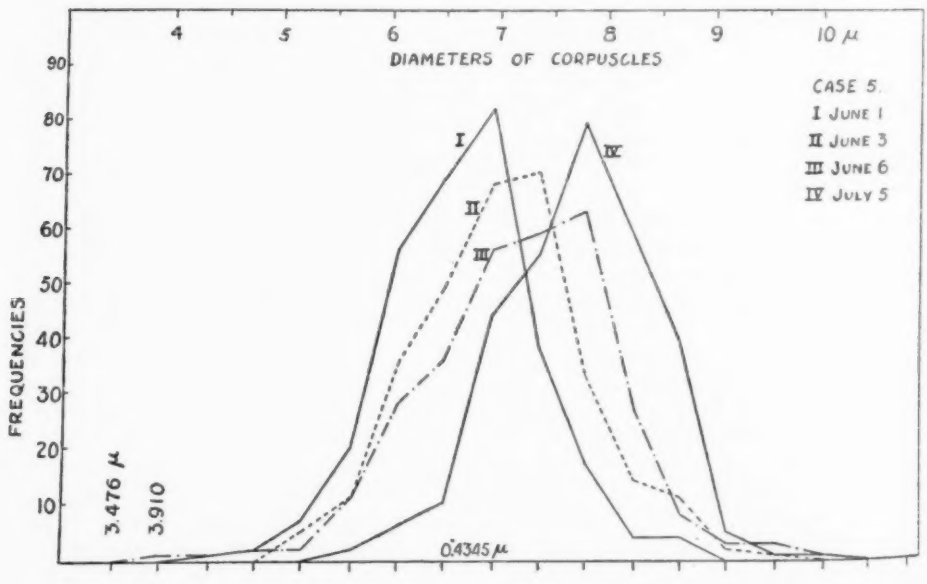

Fig. 1. Price-Jones curves of the frequency of distribution of corpuscular diameters in Case 5, made successively to show the increase in mean diameters as the patient responded to large doses of iron.

borne children and each of these described periods of anemia *following* child bearing.

Examination of all five patients revealed a palpable enlargement of the spleen. In three only the tip was felt. In two the enlargement was sufficient so that the notch could be identified. The color of the skin was abnormal enough for comment in three of the five, the description varied from sallowness, olive tinted, to bronzed. In none of the patients was there evidence of jaundice, nor of purpura. In none were the lymph nodes generally enlarged. In one case, only, the tongue was unusually smooth on its lateral borders. In no case were the neurological findings indicative of spinal cord lesions. All five patients perceived vibration perfectly.

One patient had a chronic deforming arthritis, with epiphyseal decalcification and periarticular changes. Faber and Gram (1) record eleven cases of such a combination of chloranemia with achylia gastrica and arthritis deformans, and comment on the frequent association of achylia and this form of arthritis.

In all cases examination of the stools failed to reveal occult blood. The gastric analyses in all cases showed no free hydrochloric acid while fasting or after a test meal. No attempt was made, however, to bring forth acid secretion by the administration of histamine. Hence, the term achlorhydria has been used rather than achylia gastrica in connection with our cases. In two patients with gastro-intestinal symptoms roentgenological examination of the gastro-intestinal tract and gall bladder failed to reveal anatomical abnormalities. The blood picture was essentially the same in each case, the outstanding feature being the low color index, about 0.5. In no case was the red cell count below 3.8 millions. The lowest hemoglobin was 36 per cent or 5.4 gm. per 100 cc. Two of the five patients showed a leucopenia. In the other cases the leucocyte counts were normal. In case 5, in which leucopenia was noted, salivary counts were done, as recommended by Isaacs (2), which showed a clear excess of salivary leucocytes indicating that the leucopenia was not of the aplastic type.

The differential counts revealed a slight relative lymphocytosis. Platelets appeared to be normal in the smears, and there was no evidence of platelet deficiency in bleeding or clotting mechanisms. There was very little poikilocytosis. Anisocytosis was definite but in no case extreme. Polychromatophilia was observed before treatment only in case 5, the patient having taken larger amounts of liver extract No. 343 before coming under observation. On the initial examination 3.7 per cent of the erythrocytes were reticulated in this case.

The serum was tested in each case for bilirubin by determination of icterus index, or the van den Bergh test, or both. In no case was an excess found.

The data for Price-Jones curves of the frequency of distribution of corpuscular diameters are given in tables I, II, and III. The mean diameters of corpuscles in these three cases before treatment were 6.30, 6.45, and 6.68 microns, respectively. As a result of counts of 10,000 cells in 20 normal individuals Price-Jones gives the nor-

mal mean diameter as 7.21μ. After the color index had risen in response to iron administration the mean diameters of the same three cases were 7.36, 7.51, and 7.75 respectively. The Price-Jones curves of cases 5 have been presented graphically in Fig. I., showing clearly the effect of increasing hemoglobin content upon cell diameters.

Treatment:

Four of the five patients were first treated with liver extracts or by addition of liver to the diet.

The first patient took ½ lb. of liver three times a week for nearly two years. At first there was a moderate increase in hemoglobin but at the end of the period the blood count was practically at the starting level, with a very low color index. The third patient likewise took liver over a considerable period with some improvement in both red count and color index, which was slight compared with the changes that occurred after administration of Blaud's pills in large doses. The second patient was given a "secondary anemia extract" of liver, which was found to be potent in causing regeneration of blood in the chronic post-hemorrhagic anemia of dogs in the experiments of Whipple, Robscheit-Robbins and Walden (15). This extract produced no signs of regeneration in case 2. The fifth patient was intensively treated with liver extract 343 (Lilly) and also with "ventriculin," an extract of stomach introduced by Sturgis and Isaacs (11), without curative effect. The presence of an increase in reticulocytes was the only observed effect of this treatment.

The *response to iron,* given in large doses in the form of Blaud's pills or Vallet's mass of ferrous carbonate, was clear cut and prompt in all cases. By analysis the Blaud's pills used contained in each 29 mg. of iron, so that in giving 12 pills daily approximately 350 milligrams of iron were given. This amount of iron is ten times the amount found by Sherman (10) in that American dietary richest in iron, and fifty times the poorest, and at least twenty times the amount generally sufficient for the maintenance of normal men.

The mechanism by which the administration of this excess of iron produces its curative effects in chlor-anemias, has long been a subject of speculation and study. A review of the many opinions and observations is impossible. The most recent developments in connection with iron metabolism notably the discovery by a group of workers in Wisconsin, in association with Steenbock and Hart (13), that copper in small amounts is an essential to the utilization of iron in the nutritional anemia of rats. These authors were unable to secure curative effects when purified iron salts were administered. If copper were present in small amounts as an impurity, or were added to the purified iron salts, prompt curative effects of iron were obtained. In this connection it is important to note that the Blaud's pills used by us were found by analysis to contain 0.03 mg. of copper per pill, so that *our patients received* 0.36 *mg. Cu. per diem when Blaud's pills were given.*

We have been unable to find other studies of the effect of iron in which the presence of copper has been ex-

cluded. The experiments of Whipple and Robscheit-Robbins (16), would indicate practically no curative effects of copper added to the basic diet plus a salt mixture without iron, given to dogs rendered chronically anemic by hemorrhage. On the other hand, the presence of copper as an impurity in the iron salts administered is probable.

One remaining feature is of interest. Many years ago, Romberg (9) called attention to the fact that there is a high content of water in the tissues of chlorotics. Two of our patients, who were not edematous, lost 17 and 30 lbs. of weight respectively, after the completion of the iron therapy.

Conclusions

1. Five cases of chlorotic anemia, with achlorhydria, palpable spleens, anemia with low color index and corpuscles of small mean diameters, are described.

2. Treatment with liver and liver extracts produced little or unsatisfactory curative effects.

3. Treatment with large doses of inorganic iron in the form of Blaud's pills or Vallet's mass was strikingly and promptly effective.

4. Price-Jones curves of the frequency of distribution of diameters of red corpuscles reveal abnormally small mean diameters, and that these increase to normal as the color index rises in response to treatment.

5. The preparations of iron used contained copper as an impurity.

Bibliography

[1] Faber, K., and Gram, H. C.: Relations between Gastric Achylia and Simple and Pernicious Anemia. Arch. Int. Med., 34:658. 1924.

[2] Isaacs, R., and Danielian, A. C.: Maintenance of Leucocyte Level and Changes During Irradiation. Am. J. Med. Sci., 174:70. 1927.

[3] Kaznelson, P., Reimann, F., and Weiner, W.: Achylische Chloranaemie. Klin. Wchnschr., 8:1071, June 4, 1929.

[4] Minot, G. R., and Murphy, W. P.: Treatment of Pernicious Anemia by a Special Diet. J.A.M.A., 87:470, 1926.

[5] Minot, George R.: Oxford Medicine. Vol. II, p. 600-603. Oxford Univ. Press. New York, 1920.

[6] Pearl, Raymond. Introduction to Medical Biometry and Statistics. W. B. Saunders, Philadelphia, 1923 pp. 264-293.

[7] Price-Jones, C.: The Diurnal Variation in the Sizes of Red Blood Cells. J. Path. Bact., 23:371, 1920.
Anisocytosis with Special Reference to Pernicious Anemia. Guy's Hospital Reports, 74:10, 1924.

[8] Robscheit-Robbins, F. S., and Whipple, G. H.: Blood Regeneration in Severe Anemia, II. Favorable influence of Liver, Heart, and Skeletal Muscle in Diet. Am. J. Physiol., 72:408, 1925.

[9] Romberg, E.: Bemerkungen über Chlorose und ihre Behandlung. Berl. Klin. Wchnschr., 1897:559, Nos. 25-26.

[10] Sherman, H. C.: Iron in Food and Its Function in Nutrition. Bull. 185. U. S. Dep't. Agric., Washington, D. C., Gov't. Print. Office. 1907.

[11] Sturgis, C. C., and Isaacs, R.: Dessicated Stomach in the Treatment of Pernicious Anemia. J. A. M. A., 93:747, 1929.

[12] VanSlyke, D. D., and Neill, J. M.: The Determination of Gases in Blood and Other Solutions by Vacuum Extraction and Manometric Measurement. I. J. Biol. Chem. 61:523, 1924.

[13] Waddell, J., Steenbock, H., Elvehiem, C. A. and Hart, E. B.: Iron in Nutrition. J. Biol. Chem., 77:769, 1928.
ibid. 77:777, 1928.
ibid. 77:797, 1928.

[14]WADDELL, J., STEENBOCK, H., and HART, E. B.: Iron in Nutrition, IX. J. Biol. Chem., 83:251, 1929.
ibid. 84:115, 1929.

[15]WHIPPLE, G. H., and ROBSCHEIT-ROBBINS, F. S., and WALDEN, G. B.: Blood Regeneration in Severe Anemia, XXI. A Liver Fraction Potent in Anemia Due to Hemorrhage. Am. J. Med. Sci., 179: 628, 1930.

[16]WHIPPLE, G. H. and ROBSCHEIT-ROBBINS, F. S.: Blood Regeneration in Severe Anemia, XVII. Influence of Manganese, Zinc, Copper, Aluminum, Iodine and Phosphates. Am. J. Physiol., 92:378, 1930.

The Blood Platelets in Pernicious Anemia After Liver Therapy*

By Savas Nittis, *Ann Arbor*

ALL morphological constituents of the blood in pernicious anemia show quantitative changes with the onset of a remission.

The present study deals with the changes in the numbers of the blood platelets in the relapse and during the development of remissions induced by liver therapy.

Methods of Study

In the beginning of this study different so-called "wet methods" for counting blood platelets were employed. They were soon found to be difficult to execute and inconsistent in their results. A "dry method" was then employed that not only gave fairly satisfactory results but also had the advantage of permitting the counts to be carried out at any convenient time, and the specimens could be kept on file for future reference. As there was no attempt made to record the exact number of the blood platelets present, but only to notice the relative changes in their number, the counts were carried out on the smears prepared for the routine study of the blood of the patients in this Institute.

The films were prepared as follows: Brilliant cresyl blue in 0.3% alcoholic solution was spread on clean cover-slips that had been kept in ether, and allowed to dry. The dye side of the cover-slip was then polished on typewriter paper. A drop of blood was then placed near the edge of a clean cover-slip which was inverted and placed over the cover-slip which had been prepared with the dye. After the blood had spread evenly between the slips to their edges, and the stain was well mixed with the blood, they were pulled apart and allowed to dry. They were then counterstained with the Wright's stain and mounted with Canada balsam or gum dammar.

The number of platelets accompaning one thousand red blood cells was noted. This number multiplied by the number of thousands of the red blood cells present in a cubic millimeter was taken as the total number of the blood platelets in a cubic millimeter. Since the platelets are not always distributed evenly upon a film, the microscopic field was limited so that many spots could be used. Counting was done on more than one film. The four corners, the middle and intermediate spots were always used. To avoid conscious selections of spots the eye was taken off the microscope while shifting the film

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for new fields. No field was abandoned unless it was impossible to count either of the elements. Effort was made to make an accurate count even when a congested area was met. Counts with this method and with two wet methods (Hayem, and Rees and Ecker) compared fairly well in both healthy and sick individuals, as the following count from a case of hemolytic icterus shows:

Red blood cells	2,800,000.	
Blood Platelets	142,000.	(Hayem)
	134,000.	(Rees and Ecker)
	147,000.	(Dry smear count)

The exact number of the blood platelets in the healthy individual is not as yet agreed upon. The majority of the authors give it as between 200,000 and 300,000 per cubic millimeter, although figures as low as 150,000 and as high as 500,000 per cubic millimeter are quoted in the literature as normal. The method here employed gave fairly constant figures for the same individual in many successive counts, but varied considerably from person to person. The figures below, representing counts from two healthy male persons of the same age, members of the staff of this Institute, made on corresponding days by the same technic and technician, emphasize these variations in different individuals.

All counts in the healthy individuals showed the variation in the blood platelet count to be greater than the red or even the white blood cell count. But however inaccurate these figures may be, they are of comparative value, although possibly to a less degree than the white or red blood cell count. All smears were made by the same individuals, employing the same technic, and all platelet counts were made by the same person. This eliminated, to a certain degree, personal errors.

Data

It was observed that the number of the blood platelets in pernicious anemia before starting treatment was always less than the lowest given normal count. Their number appeared to be inversely proportional to the degree of anemia present but this did not seem to follow a definite rule. When the red blood cell count was below one million the platelets were found to be below 100,000 and at times even less than 10,000. (Table I). It was observed however that with this same technic the number of the blood platelets were found in some cases to be less than 100,000 even after remission and for many days following it. (Chart I). But irrespectively of the initial number of the blood platelets there followed a rise after effective liver therapy. This rise occurred either before (Table II, Chart I), with (Table III, IV and V), or after (Chart II, Table I and VI) the reticulocyte rise, but always before the rise of the blood cells. In cases where the platelet rise preceded that of the reticulocytes there was usually another rise, at times higher than the first, oc-

S. N.					
Red blood cells	5,560,000	5,810,000	5,840,000	6,430,000	6,050,000
Blood platelets	302,000	255,000	280,000	289,000	314,000
M. R.					
Red blood cells	5,630,000	5,670,000	5,350,000	5,560,000	5,590,000
Blood platelets	170,000	119,000	113,000	189,000	122,000

curring several days after the reticulocyte rise. (Table V). The rise in the number of the blood platelets was a constant phenomenon but in no two cases appeared exactly alike. It did not follow as definite a law as the red blood cell count and the hemoglobin or as the reticulocyte percentage. The fluctuations in their number were as irregular as those of the white blood cells. No gross correlation was observed to exist between the red blood cell, the reticulocyte forms or the white blood cells. Like the red and white blood cells, the platelets were decreased during relapse. In some cases a high platelet count, as compared to the count found in the initial stage of the disease, was found at a second relapse (Table III). Again like the red and the white blood cells they showed a rise during either a spontaneous remission or one induced with liver therapy. But unlike both these elements, they increased beyond the normal level, at times reaching three or four times

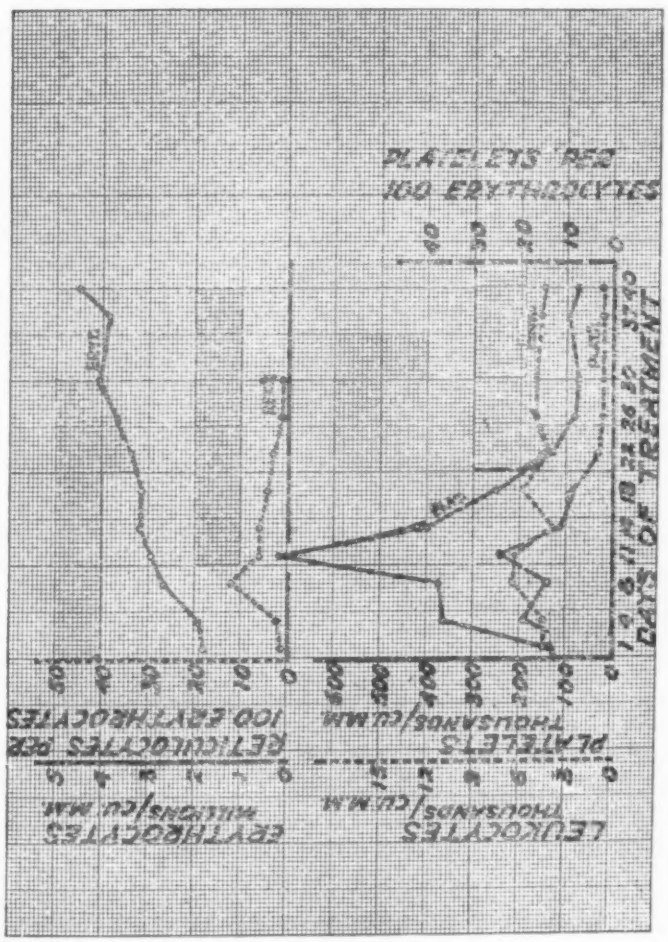

CHART I

the normal count (Table III and V), and then decreased. The drop was as irregular as the increase and in some cases it did not stop at the normal level but went below it. (Chart I, Table IV). In a few cases, for many days following remission the blood platelet number continued to be below the normal level (Table IV, Chart I). In other cases it was slightly above this (Table II) and in some cases it corresponded to the counts found in normal individuals. The variations in the number of the blood platelets present before commencement of treatment appeared to be independent of the clinical picture of the disease and likewise patients with parallel responses in the blood platelets during the progress of liver therapy showed no marked apparent similarity in the improvement of the clinical symptoms.

Of interest is the case presented in Table I. To this patient 30 bottles of Lilly's liver extract, made from 3000 grams of liver were given by means of

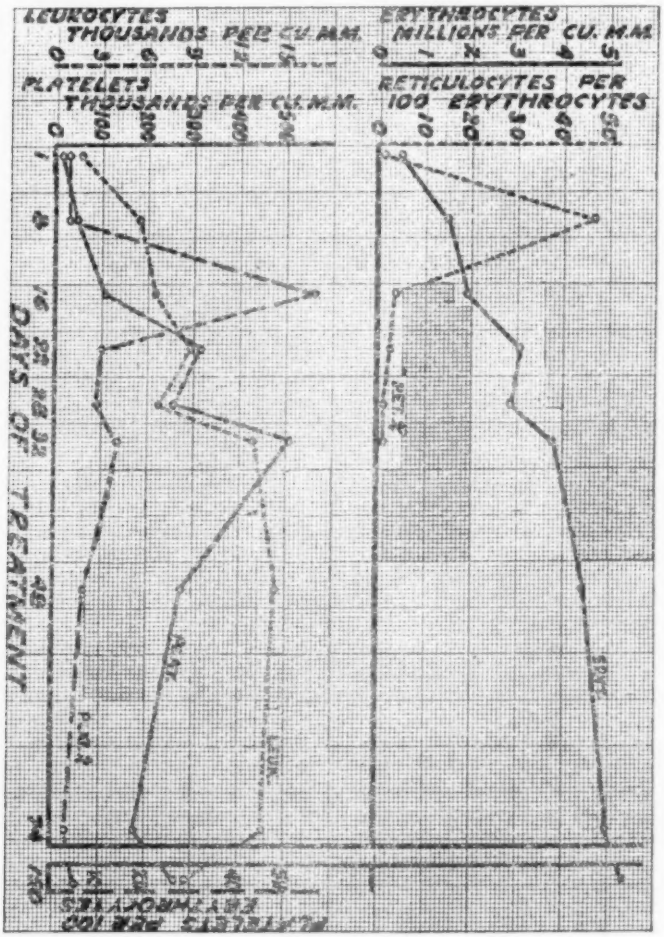

CHART II

TABLE I.

Days of Treatment	Erythro. Millions per cu. mm.	Hemoglobin % (Sahli)	Reticulocyte %	Leukocytes per cu. mm.	Platelets per cu. mm.	Platelets per 100 Erythrocytes
	.710	13	1.6	4,500	22,000	3.2
1	.690	15	2.1	4,900	18,000	2.6
2	.402	12	.9	4,160		
3	.690	12	2.5	9,960	8,000	1.2
4	.720	12	16.0	22,000	6,000	.8
5	1.190	18	42.0	8,800	5,000	.4
6	1.400	20	45.0	4,750	8,000	.6
7	1.590	29	27.0	3,800	22,000	1.4
8	1.710	33	20.0	6,400	65,000	3.8
9	1.360	28	11.7	6,550	106,000	7.8
10	1.590	29	4.7	5,950	159,000	10.0
11	1.780	34	1.3	3,700	256,000	14.8
12	1.530	30	.6	2,650	186,000	12.2
13	1.990	30	.4	1,550	314,000	15.8
14			.1			
17	1.480	30	1.1	2,850	62,000	4.2
20	1.980	30	4.2	3,000	67,000	3.4
24	1.750	40	4.8	5,800	112,000	6.4
27	1.330	43	2.5	11,500	88,000	6.4
31	1.820	40	1.	4,400	386,000	21.2
33	2.400	42	1.	6,250	500,000	20.4
76	3.600	78	1.	5,150	317,000	8.8
6 Mo.	4.900	90		9,550	632,000	12.9
12 Mo.	5.450	93		7,900	518,000	9.5

a stomach tube on the first day of treatment. No more liver was given for twelve days. The platelet count which was very low, rose from an average of 10,000 per cubic millimeter to 314,000 per cubic millimeter thirteen days following the administration of the liver extract. The highest reticulocyte percentage was found on the seventh day following the administration of the liver. On the thirteenth day 30 capsules of liver extract, representing 480 grams of fresh liver, were given. This dose was repeated daily thereafter. From the thirteenth to the thirtieth day the platelets were below 100,000 per cubic millimeter, then they increased again reaching 500,000 on the 33d day. This second and higher rise might be related to the second reticulocyte rise which on the 24th day was 5%. After twelve months the platelets were still above 500,000 per cubic millimeter. In this, as in all tables and charts published here, the counts were made daily. The intermediate counts were omitted from the tables in the interest of clarity and economy of space.

In most cases the blood platelets during the initial period of the disease or during relapse were usually of a very small size. At times, however, platelets of larger size were observed and in some cases also giant forms. Following remission induced with liver

TABLE II.

Days of Treatment	Erythro. Millions per cu. mm.	Hemoglobin % (Sahli)	Reticulocyte %	Leukocytes per cu. mm.	Platelets per cu. mm.	Platelets per 100 Erythrocytes
1	1.220	22	.8	4,800	167,000	13.8
3	1.370	23	1.5	3,250	559,000	40.8
5	1.260	26	8.1	4,150	247,000	20.4
6	1.240	26	17.8	2,850	79,000	6.4
7	1.166	26	25.6	2,360	156,000	9.4
8	1.990	35	16.6	2,250	242,000	12.6
9	2.650	39	10.5	3,150	234,000	12.6
10	2.660	42	4.4	3,950	293,000	11.0
11	2.370	44	5.7	4,500	223,000	9.4
12	2.170	48	6.0	5,050	295,000	13.6
13			2.4			
14	2.570	52	6.2	4,100	264,000	10.2
15	2.760	52	9.1	3,550	502,000	18.2
17	3.460	51	2.3	6,150	623,000	18.0
20	3.100	49	.2	3,750	322,000	10.4
26	4.030	66	1.	6,950	572,000	14.2
29	3.930	60	1.	4,350		
60	5.270	60		10,300	857,000	16.2
200	4.950	76		9,550	416,000	8.4
300	4.890	78		7,550	398,000	8.2

therapy, it was observed that the size of the platelets followed a definite cycle although of an irregular rhythm. The giant forms, which at times were of the size of normal erythrocytes, were followed by the appearance of medium sized platelets, which in turn were followed by the appearance of small platelets, at times of a very minute size. This period was then followed by a shower of larger and giant forms. This was not a constant phenomenon and the cycle was not very regular.

SUMMARY

In pernicious anemia the blood platelets are decreased in number but not as uniformly as the red blood cells.

Following remission induced by liver therapy the platelets increase in number, reaching a level higher than normal, after which they decrease. The highest count usually occurs several days after the maximum reticulocyte percentage is reached.

There is no gross correlation between the increase in numbers of the platelets and that of the erythrocytes, the reticulocyte percentage or the number of leukocytes.

Giant forms of blood platelets appear and disappear at intervals in all cases but this phenomenon does not form a markedly regular rhythm.

TABLE III.

Days of Treatment	Erythro. Millions per cu. mm.	Hemoglobin % (Sahli)	Reticulocyte %	Leukocytes per cu. mm.	Platelets per cu. mm.	Platelets per 100 Erythrocytes
1	.200	27	1.	3,500	97,000	8.1
2	.730	27	1.	3,550	71,000	9.8
3	.970	26	2.3	5,030	40,000	4.7
4	.875	27	2.9	2,700		4.7
5	1.000	32	4.3	4,000	50,000	5.0
6	.960	32	6.9	3,200	121,000	12.6
7	1.080	32	11.6	3,900	229,000	21.2
8	1.250	42	8.7		273,000	23.5
9	1.095	50	8.9	4,050		
10	1.080	45	13.3	4,450	330,000	30.6
11	1.195	42	16.	4,000	459,000	38.4
12	1.200	44	9.7	5,650	343,000	28.6
13	1.585	41	15.8	5,050	500,000	31.6
14	1.420	44	9.6	5,050	408,000	29.4
15	1.310	46	5.3	6,050	498,000	38.0
16	1.520	41	3.7	6,550	638,000	42.0
17	1.755	47	7.6	5,150	629,000	36.0
18	1.360	52	3.2	5,800	571,000	42.0
20	1.810	53	1.4	5,000	860,000	47.4
22	2.100	63	1.6	6,450	676,000	32.2
24	2.550	62		5,400	770,000	30.2
48	3.500	76		4,250	1,225,000	35.0
78	5.040	84		10,850	554,000	11.0
124	5.980	83		11,550	478,000	8.0
9 Mo.	2.500	50		12,050	250,000	10.0
18 Mo.	2.800	71		7,250	487,000	17.4

TABLE IV.

Days of Treatment	Erythro. Millions per cu. mm.	Hemoglobin % (Sahli)	Reticulocyte %	Leukocytes per cu. mm.	Platelets per cu. mm.	Platelets per 100 Erythrocytes
1	1.09	19	1.2	2,350	21,000	2.0
3	.77	18	1.3	3,100	42,000	6.4
9	1.63	32	32.0	2,900	563,000	34.6
17	3.06	41	1.9	5,550	222,000	7.4
32	3.80	65	1.7	6,400	38,000	1.0
43	3.38	70		9,350	155,000	4.6
47	4.60	71		8,000	156,000	3.4
66	5.39	70		10,250	5,000	0.1
7 Mo.	5.15	88		17,250	227,000	4.4
20 Mo.	4.94	90		9,000	504,000	10.2
27 Mo.	4.24	95		5,300	301,000	7.1

TABLE V.

Days of Treatment	Erythro. Millions per cu. mm.	Hemoglobin % (Sahli)	Reticulocyte %	Leukocytes per cu. mm.	Platelets per cu. mm.	Platelets per 100 Erythrocytes
1	1.49	38	1.9	4,300	89,000	6.0
2	1.69	41	2.6	2,800	60,000	3.6
3	1.59	37	1.7	2,290	73,000	4.6
4	1.49	36	3.0	3,550	220,000	14.8
5	1.89	40	4.6	4,050	108,000	5.8
6	1.76	42	8.1	3,900	211,000	12.0
7	2.02	43	9.7	5,900	157,000	7.8
8	1.90	47	15.2	6,840	213,000	11.2
9	1.66	52	4.9	5,050	803,000	48.4
10	1.94	52	9.3	6,300	608,000	31.4
11	1.89	52	6.4	6,700	665,000	35.2
12	1.86	52	9.1	6,650	681,000	36.6
13	2.67	62	6.0	6,200	844,000	31.6

TABLE VI.

Days of Treatment	Erythro. Millions per cu. mm.	Hemoglobin % (Sahli)	Reticulocyte %	Leukocytes per cu. mm.	Platelets per cu. mm.	Platelets per 100 Erythrocytes
1	0.83	19	2.4	3,350	50,000	6.0
8	1.38	27	25.3	4,500	113,000	8.2
16	2.65	42	2.9	5,750	530,000	20.0
21	2.22	49	1.	8,350	543,000	20.4
24	2.98	49		4,800	745,000	25.0
27	3.49	60		7,600	419,000	12.0
30	2.92	60		6,200	350,000	12.0
33	2.88	60		6,350	127,000	4.4
36	4.11	58		8,100	370,000	9.0
39	4.19	59		5,500	168,000	4.0
42	3.87	71		8,350	193,000	5.0
45	3.58	64		9,450	358,000	10.0
48	4.10	69		9,550	615,000	15.0
72	4.88	75		12,200	390,000	8.0
118	5.34	76		7,250	246,000	4.6

Clinical Consideration of an Anemia of Pregnancy and the Puerperium*

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PUERPERAL anemia, which is probably a continuation if not a progression of the anemia of pregnancy, was first described by Channing in 1842,[1] and for many decades doubted as being a specific anemia, has received more study in the past two decades and has been established as a definite anemia related to pregnancy and the puerperium; and furthermore according to Murdock's[2] observations, "if the patient survives the acute attack, the blood picture usually returns to normal."

For an anemia to merit such a classification, we contend that all anemias should be excluded which might be explained by hemorrhage, sepsis (including infections), nephritis, syphilis, previously present hemolytic icterus, or primary pernicious anemia, leukemia, acute or chronic, myelocytic, or lymphocytic; in other words, all possible causes except the pregnancy itself. We also wish to exclude the so-called toxemia of pregnancy as it is generally known, unless the anemia we are discussing is a manifestation of a toxin produced by the pregnancy.

A most comprehensive clinical picture of this anemia is given by Rowland:[3] "An insidious onset of anemia in the latter weeks of pregnancy, often not recognized till in the puerperium, usually antepartum symptoms of weakness, breathlessness on exertion, palpitation, headaches, dizziness, edema of the feet, and occasionally an *associated* definite toxemia of pregnancy with albuminuria and hypertension. Labor may come on prematurely, is characteristically short, and relatively painless. Still-birth may occur, but a living child does not share in the anemia and develops normally. Labor aggravates the anemia, and the patient may go into collapse at once if the anemia is marked. Typically there is a rapid progression in the anemia for the first week or two. Or, it may be slow, requiring two months before recognition. Hematologically primary and hematologically secondary."

Esch[4] insists "the secondary type never goes into the primary type, and that however closely the picture may resemble pernicious anemia, no authentic case of recurrence independent of pregnancy has yet been reported." Such views are in accord with our findings, as a later analysis will show.

In considering the differential diagnosis, the relationship of this anemia to pernicious anemia is often very close. Achlorhydria may be present with diarrhea, sore tongue, paresthesia

in the extremities, and a blood picture closely resembling primary anemia. The very fact that liver extract is helpful in selected cases argues a closer kinship than could have been claimed before. Pepper[5] admits, "unquestionably the evidence favors the view that the anemia is a hemolytic anemia, but no evidence to permit us to designate the hemolytic factor at work." If we accept the theory that pernicious anemia is a deficiency disease, which deficiency is supplied by liver extract, might not certain of the anemias of pregnancy and the puerperium be due to the same but temporary deficiency? We say temporary, because it is generally admitted that when the patient is tided over the acute attack, she will probably remain well—succeeding pregnancies may or may not provoke another attack.

If the anemia of pregnancy is not a toxemia of pregnancy, the resemblance is so close that some of our patients have been sent in as a toxemia for induction of premature labor or Caesarian section. The symptoms of toxemia are the albuminuria, anemia, increased pulse rate, edema, and sometimes hypertension. All of these findings may be present in the anemia of pregnancy. The actual diagnosis may not be made until after the pregnancy has been terminated and the patient fails to make the expected recovery. If the anemia of pregnancy is kept in mind and the condition of the patient justifies the delay, the treatment of the anemia may be instituted and the patient probably carried to term.

The presence of fever, frequently alarmingly pronounced, gives the obstetrician much concern, fearing puerperal sepsis. If the case is seen and a diagnosis made before labor, the rise of fever can be prognosticated, and this gives the obstetrician and patient much comfort when there is a persistent elevation of fever after delivery. The ultimate exclusion of sepsis will not be made by the negative blood cultures, which frequently leave one in doubt, but by the rapid fall in temperature and leucocytosis, if present, as the anemia improves under treatment. The absence of leucocytosis does not necessarily eliminate sepsis as a diagnosis, because Cabot[6] and Osler have shown by four autopsy cases that a severe sepsis may be present without including any leucocytosis.

The excessive amount of albumin in the urine would lead the unwary to make a diagnosis of uncomplicated nephritis. We feel that we have made that mistake more than once, with attention and treatment focussed entirely on the nephritis, when, if the anemia had been treated, the albuminuria would have cleared up.

We have nothing distinctive to offer regarding this albuminuria, but suggest that a study of the anemia will most likely indicate the condition requiring the treatment, and the therapeutic response will verify the diagnosis.

If the case is first seen after the anemia has been present for some time, or was slow in appearing, the fever and pronounced cardiac murmur, usually systolic in time, suggest endocarditis. Here again, the response to the treatment of the anemia will establish the diagnosis.

The treatment will depend on the individual case, and if the proper treatment is selected and adhered to, the response is most gratifying. The

anemia might be severe and the patient so ill, that the immediate transfusion is indicated. This might suffice, but it is well to follow up with either liver extract and hydrochloric acid, if achlorhydria is present, or massive doses of iron. We have tried to demonstrate with cases all too few, that the patient without hydrochloric acid in stomach contents, or with a low acidity, will respond better to liver extract, and the patient with normal or high acidity, will not respond to liver extract, but to massive doses of iron. In our earlier cases we transfused, then gave dilute hydrochloric acid, iron, arsenic, and later when the value of liver extract in pernicious anemia was demonstrated, we used it in the treatment of puerperal anemia.

In the analysis of our twenty-two cases, eight of which were reported in 1925[7], we find it almost impossible to classify them as primary and secondary types. Seven showed involvement of the gastro-intestinal, the hematopoietic, and nervous systems (accepting the history of paresthesia as an involvement), two of the gastro-intestinal and hematopoietic. These nine we classified as of the primary type. The remaining thirteen showed such bizarre pictures as to defy classification, save that they were undoubtedly related to the pregnancy and puerperium. Of the nine cases in which gastric analyses were done, five showed no free hydrochloric acid, and in four the hydrochloric acid was below normal.

The blood Wassermann (Kolmer) was negative in eighteen cases, in four it was not done. These patients showed no clinical evidence of syphilis, so with the negative Wassermann reactions, we feel that we have contradictory evidence to syphilis playing any part in these cases.

In this particular section of North Carolina, hook-worm has been very prevalent. This required the exclusion of uncinariasis as a contributing factor in the anemia. In eleven cases

CHART. Analysis of 22 Cases.

in which the stools were studied for ova, they were found in only one, and when that patient returned with a recurrence, the ova were not present.

Fever was present in all the series of twenty-two cases. In nineteen the temperature was 100 degrees F, or over. In one 104 and another 105 degrees. The urine of eighteen showed albumin estimated as varying from i to iii on a scale of iv.

In twenty-one cases the red cell counts were below three million, in sixteen of these below two million, and in four of these below one million. The color index was greater than one in thirteen cases. In sixteen the smears showed definite anisocytosis and poikilocytosis. Nucleated reds were found only once and then there were 263 to each 100 white cells counted. This case, however, was classified as the secondary type and made no response to liver extract, but responded rapidly to 100 grains of iron daily. The white count was below 8,000 in fifteen, and ranged between 8,000 and 20,000 in the others.

Five of the cases gave histories of recurrence, two more were treated for the initial attacks and later the recurrence in the hospital. In each instance the recurrence occurred with pregnancy. The youngest gave the age of 16, and the oldest 38, average for the twenty-two, 26 years. The absence of recurrence except with the pregnancy, and the youth of the patients are distinctly against the findings in pernicious, or true Addisonian anemia.

Thirteen received transfusion. Of these two died. One of these was extremely ill on admission, and died thirty hours after transfusion with acute dilatation of the heart. The second of the transfused series to die, did not follow up treatment. The third case to die, was not transfused for lack of a suitable donor, left the hospital and refused treatment. Six made a complete recovery on liver extract alone. One did not improve on liver, but made rapid progress on 100 grains of Blaud's mass daily.

The following cases are presented as typical of the anemia, with the added features of being very severe, not responding to transfusion, but to liver extract.

Mrs. J. A. S., Hosp. No. 15,439, age 33, para V, admitted to the hospital January 4th, 1928, with the complaints of weakness, dyspnea, dizziness, and headaches.

She had noticed these symptoms for a month and a half before her baby was born. On admission, her baby was 10 days old, and her former complaints had been aggravated since its birth.

She had had high blood pressure and severe nephritis with her fourth baby. She had had three miscarriages, and one baby died at the age of two years. As a child she had had "rheumatism" and typhoid fever, but no other illnesses save child-births.

On examination she appeared well nourished, but very anemic. Her eye-grounds showed recent retinal hemorrhage. There were no cardiac murmurs, no cardiac enlargement. Her blood pressure was 130-90, pulse 100, temperature 102. The liver and spleen were both palpable. The tendon reflexes were normal, no Babinski. The uterus showed moderate subinvolution, with slight stellate tears of the cervix.

Laboratory findings: Urine; albumin ii on a scale of iv, many hyaline, granular, and cell casts. Blood: hb. 20%, red cell count 1,060,000, white cell count 16,400, polymorphonuclears 86%, lymphocytes 11%, transitionals 2%, eosinophiles 1%. The platelets were estimated as plentiful. There was marked difference in size and shape of the red cells, marked achromia, no malaria,

marked stippling and polychromatophilia. The icterus index was 20, Van den Bergh direct reaction, hemolysis of the red cells began at 0.4 and ended at 0.275. The blood urea was 32 mg., blood Wassermann negative. The feces showed no hook-worm ova, the gastric contents showed no free hydrochloric acid.

On January 6th, she was transfused with 500 c.c. of citrated blood with no reaction. On January 12th, the day she left the hospital, her red cell count was 1,890,000, hb. 40%, white cell count 9,400, polymorphonuclears 78%, lymphocytes 6%, large mononuclears 14%, transitionals 1%, eosinophiles 1%. Anisocytosis and poikilocytosis marked.

She was given dilute hydrochloric acid and liver feedings which she refused. Soon after leaving the hospital, she lost the gain she had made. Her vision became very much impaired and she developed a generalized edema. It was felt that she had not received sufficient benefit from the transfusion to repeat it. She was then put on liver extract which she tolerated better than the liver feeding. Improvement on this was very rapid. The vision improved, but never returned to normal. On April 3rd, 1930, her red cell count was 4,210,000, hb. 80%, smear showed normal red cells.

A second case of interest is case #14 in our series. Mrs. A. T. G., who was treated twice for the same condition. Was age 22 when first seen in July, 1926, at which time she complained of weakness. She was pregnant and nearly at term. General physical examination was practically negative except for the apparent marked anemia. She had 1,050,000 red cells and hb. 25%, blood Wassermann negative. Her stools contained hook-worm ova. Her temperature was 102, white count 5,000 with a normal differential (no increase in eosinophiles), urine contained albumin ii on a scale of iv. She was transfused with 500 c.c. of citrated blood and given two treatments for her hook-worm, and put on dram doses of dilute hydrochloric acid. She went to term and delivered a normal baby that is still living. She then got along alright at home until two months before her second admission in August, 1928. She was delivered of her fifth baby two months before admission, and although she lost very little blood, she had continued to get weak and pale. She was sent to us again for transfusion. This time her skin had a slightly yellowish appearance (icterus index 22) but her general physical examination was essentially negative. She was nursing her baby. Her red cell count this time was 1,350,000, with hb. 30%, and blood volume index 1.19. There was definite change in size and shape of the red cells. Her Wassermann was negative again and the stools repeatedly negative. Her hydrochloric acid was 12. The urine showed an albumin i on a scale of iv. Her blood urea was 40 mg. per 100 c.c. and kidney function 69% in two hours. Although she was fairly sick there was no emergency so we decided to try liver extract instead of transfusion. She was given one ampule of Lilly's Extract #343 after each meal. At the sixth day her red count was 2,160,000 and hb. 45%. Her appearance and feelings were much improved. On the 12th day her count was 2,460,000 and hb. 50%. The patient continued to improve at home and since then has had another baby, and her physician, Dr. Julian Brantley, of Spring Hope, N. C., stated recently that she was not anemic and had no trouble with her last pregnancy.

Discussion:

While we find that many of these cases resemble pernicious anemia very closely, there are many that do not, and yet the anemia is definitely associated with pregnancy and the puerperium. We are not able to agree with Alder[8] who states flatly "that in the history of almost every instance of the pernicious type of the anemia of pregnancy there occurs a reference to some previous chlorosis, severe anemia, syphilis, or other infection. McSwiney[9] in analysing 43 cases of various types of anemia of pregnancy was impressed with the frequent association of syphilis with the anemia. Eighteen of our patients had negative Wassermanns, (Kolmer) and the test was not made on the other four.

Aubertin 10 does not hesitate to call the condition pernicious anemia, and Brady[11] who collected 68 cases from various sources, and others, do not hesitate to term the condition "Pernicious anemia of pregnancy," however, we have not been able to find any case in the literature that meets the modern requirements for a diagnosis of typical Addisonian anemia. The etiology is obscure, and the disease is pernicious in most cases unless checked, however, one very important fact is that when recovery takes place it is permanent, with no remission and no recurrence unless at a subsequent pregnancy which does not necessarily follow, and therefore an attack successfully treated is not a contraindication to subsequent pregnancies.

We feel that the term "pernicious anemia" is loosely used; less obnoxious would probably be "A pernicious type of anemia," however, in the secondary type the patient may also have a fatal termination if not properly treated.

Unless puerperal anemia is kept in mind, the patient in almost every instance will be treated for some other complication. In our series, the red counts were so low, that the most obvious need of the patient was blood. Our early cases were all transfused provided a suitable donor could be found but in no instances did we rely on transfusion alone, although Allan[12] states that transfusion alone is curative. Knowing that transfusion is not always available and following its failure in some instances to give the desired result (case 7 and 17 of this series) we have utilized liver extract in selected cases. As stated above, transfusion may be a life saving measure, but we hope that with the early recognition of the disease that liver extract or iron may be used before the condition of the patient gets so serious as to require transfusion. We had six to make a complete recovery on liver extract alone. In the literature liver extract has been used successfully by Brault[13], Larribere[14], Peterson[15] and others.

In conclusion we believe that there is an anemia of pregnancy and the puerperium that is a definite clinical entity. That in some instances it closely resembles pernicious anemia but not true Addisonian anemia. The indications for treatment are definite and the response is very satisfactory.

BIBLIOGRAPHY

[1]Channing, W.: New England Quart. Jour. Med. & Surg., 1842, 1, 157.

[2]Murdock, T. P.: Ann. Int. Med., 1927, 1, 133.

[3]Rowland, V. C.: Ann. Int. Med. 1927, 1, 129.

[4]Esch: Zentralbl, f. Gynäk, 50, 857.

[5]Pepper, O. H. P.: Med. Clin. N. A., 12, 932.

[6]Cabot & Osler: Med. Clin. N. A., 12, 927.

[7]Smith, C. T.: Surg. Gyn. & Obst., 1925, 40, 223.

[8]Alder: Zeitschr, f. Geburtsch, u, Gyn., 1924, 87, 505.

[9]McSwiney: Indian Med. Gaz., 1927, 62, 487.

[10]Aubertin: Le Bull. Med. 1925, 39, 261.

[11]Brady: These Paris, 1923-24.

[12]Allan, Wm.: South. Med. Jour. 1929, 22, 624.

[13]Brault, P.: Bull. de la Soc. d'Obs. & Gyn. Paris, March 1928.

[14]Larribere: Bull. de la Soc. d'Obs. & Gyn. Paris, April 1928.

[15]Peterson: J. A. M.A., 1930, 94, 839.

Variations in Pulse and Blood Pressure With Interrupted Change of Posture*

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CAREFUL studies of the normal circulatory response to uninterrupted changes of posture from recumbency to standing have been previously reported[4,5,6]. Following Ghrist and Brown's report of a step-like fall of both systolic and diastolic blood pressure, with associated faintness or syncope on passive, interrupted change of posture from recumbency to standing in one case of postural hypotension with syncope and in one case of proved Addison's disease, it was deemed advisable to repeat these fractional postural studies on groups of normal subjects and of patients. The following study of pulse rate, blood pressure and resultant symptoms from passive postural change, both interrupted (in all persons) and uninterrupted (in thirty-two of the entire number), represents observations carried out on forty normal persons (twenty-three females and seventeen males) and on 108 registered patients at The Mayo Clinic and its allied hospitals. The mean results of all these determinations are presented in the accompanying table. The normal persons studied were mainly of three occupations: physicians, technicians and secretaries. The conditions of the patients chosen for study are classified in the following main groups: (1) hypotension; systolic blood pressures of 100 mm. of mercury or less; (2) benign (essential) hypertension; systolic blood pressures of 140 mm. or more; (3) malignant (essential) hypertension; (4) postural hypotension with syncope; (5) postural weakness or dizziness; (6) diabetes mellitus; (7) nonpostural weakness or dizziness; (8) Addison's disease; (9) chronic infectious arthritis†; (10) Raynaud's disease,† and (11) scleroderma. When individual cases were included in more than one group, this is indicated.

Method

All determinations of pulse and blood pressure were carried out by me, over a period of thirty-three months, in the same room, at hours varying from 11 a.m. to 8 p.m. The subjects were made to lie horizontally on a roentgenographic table (180°) for periods of from three to fifteen minutes, until two consecutive readings of

*Abridgement of thesis submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Medicine, 1930.

†Certain of these were studied before and after sympathetic ganglionectomy and trunk resection.

blood pressure fell within 2 mm. of each other, in both systolic and diastolic levels. An upright mercury standard type of blood pressure apparatus was used in all determinations, with the cuff applied to the upper part of the right arm of the subject and the calibrated mercury scale standing at the approximate level of the subject studied. The mechanism was explained to the subjects before the test was begun in order to reduce the element of apprehension to a minimum. After the blood pressure had agreed within 2 mm. (both systolic and diastolic) the pulse was determined for fifteen seconds and the last reading of blood pressure and the associated pulse rate were recorded. The subject was then moved to posture 2 (157.5°) by use of the electric motor attached to the table. Determinations of blood pressure and pulse rate were then taken at the new posture. The same procedure was carried out at 135°, 112.5° and 90°* (erect) in sequence as indicated. The time elapsing between determinations at posture 1 and posture 5 averaged about five and a half minutes.

When uninterrupted determinations of pulse and blood pressure were made, the same general procedure was carried out, with the exception that the motor, and motion of the table, were not allowed to stop between postures 1 and 5. The time elapsing between determinations at posture 1 and at posture 5 was approximately two minutes in the uninterrupted tests. The mean average results in the groups studied are presented in the tabulation.

*The more exact angle of the erect posture with the table used measured 93°. For the purpose of clarity, the approximate figure, 90°, will be used in the tables, graphs, and so forth.

Comments and Consideration of Results

The average normal circulatory responses to passive change from recumbency to the erect posture are: (1) rise of pulse rate; (2) rise of diastolic blood pressure (a probable index of vasomotor tonus), and (3) slight fall or stationary maintenance of the systolic blood pressure (fig. 1). The mechanisms by which these effects are accomplished are as follows: (1) decrease of the venous return incites the cardiac mechanism to increased rate in order to maintain equality of cardiac output in the upright posture, and (2) through the agency of vasomotor stimulation, a vasopressor response takes place in the peripheral circulation (splanchnic area especially) to oppose the hydrostatic effect of gravity, and to maintain sufficient diastolic level to preclude anemia of the brain. Defective vasomotor tonus may arise from: (1) paralysis, inhibition or dysfunction in the nervous mechanism of vasomotor control, which in turn is influenced by the circulating hormones of glandular secretion; (2) atony or paralysis of the myoneural juncture in the peripheral (especially splanchnic) vessels, or (3) changes in the character of the walls of the blood vessels themselves. Some compensation for these defects may or may not be obtained by tonus of abdominal muscles and increase of respiratory movements which oppose splanchnic congestion and facilitate venous return.

In the course of interrupted, passive change from recumbency to the erect

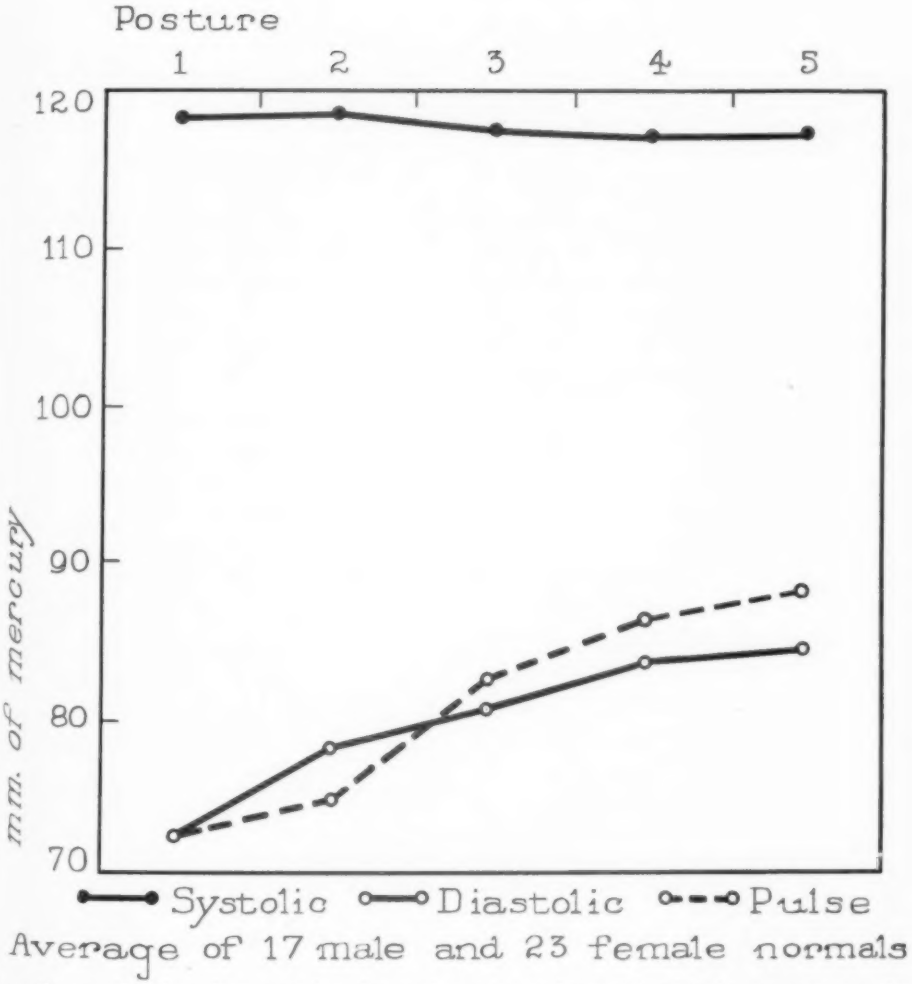

FIG. 1. Results of progressive change in posture of normal subjects; seventeen males and twenty-three females. The postures are designated as follows: (1) supine or 180°; (2) 157.5°; (3) 135°; (4) 112.5°, and (5) erect or 90°.

position, from which the following estimations of the average normal response were made, the pulse should rise approximately fifteen beats each minute, the systolic blood pressure should remain approximately unchanged (average fall 1 mm.) and the diastolic pressure should rise approximately 12 mm. in a group of normal adults aged approximately twenty-seven and two-tenths years. Individual normal subjects may vary considerably above or below these average determinations. No pertinent fall of diastolic blood pressure took place during any of the determinations on normal subjects, although three of these subjects exhibited falls of 4.2 and 2 mm. of diastolic blood pressure, respectively. The presence of definite hypotension, along with undernourishment, did not preclude approximately normal response of blood pressure to passive postural change in the group of eleven such cases studied.

A representative group of twenty cases of benign (essential) hypertension (fig. 2) exhibited instability of systolic blood pressure on postural change, which appears to indicate the presence of remaining flexibility in the peripheral resistance at high pressures. The same persons reacted with subnormal rise of diastolic pressure on postural change, which gives evidence of pre-existent vasospasm or inelasticity, or both, in the peripheral vascular system.

The ten cases of malignant (essential) hypertension (fig. 3) as a group gave evidence of less flexibility in the peripheral vascular system than the cases of benign hypertension. The reactions in these cases yielded physiologic evidence of severe, inflexible arteriolar constriction, corroborating the previous contentions of Kernohan, Anderson and Keith. Also, the circulatory adjustment of these patients to postural change is accomplished with less rise of pulse rate than in those who are normal or who have benign hypertension. This has two possible explanations: the struggle of the circulatory mechanism against its severe basal load and cardiac hypertrophy of such magnitude as to accomplish slight physiologic adjustment with less change of rate, provided cardiac reserve is relatively adequate*.

On postural test the series of six cases in which there was generalized (senile) arterioclerosis gave evidence of less peripheral flexibility and less vasomotor tonus than the group with benign hypertension.

There was marked fall of systolic and diastolic blood pressure with unchanging pulse rate in Ghrist and Brown's previously reported case of postural hypotension with syncope. In their case, evidently atony in the myoneural juncture of the splanchnic arterioles was the main cause of failure in the mechanism of vasomotor tonus. Successful treatment of the patient by repeated doses of ephedrine gave striking corroboration of the above contention.

*Seven of these cases in which the electrocardiograms were significant of myocardial degeneration gave evidence that instability of their systolic blood pressure cannot be explained on the basis of a defective myocardium. The failure of the diastolic blood pressure to rise on postural change also was not confined entirely to those cases in which there was electrocardiographic evidence of myocardial degeneration.

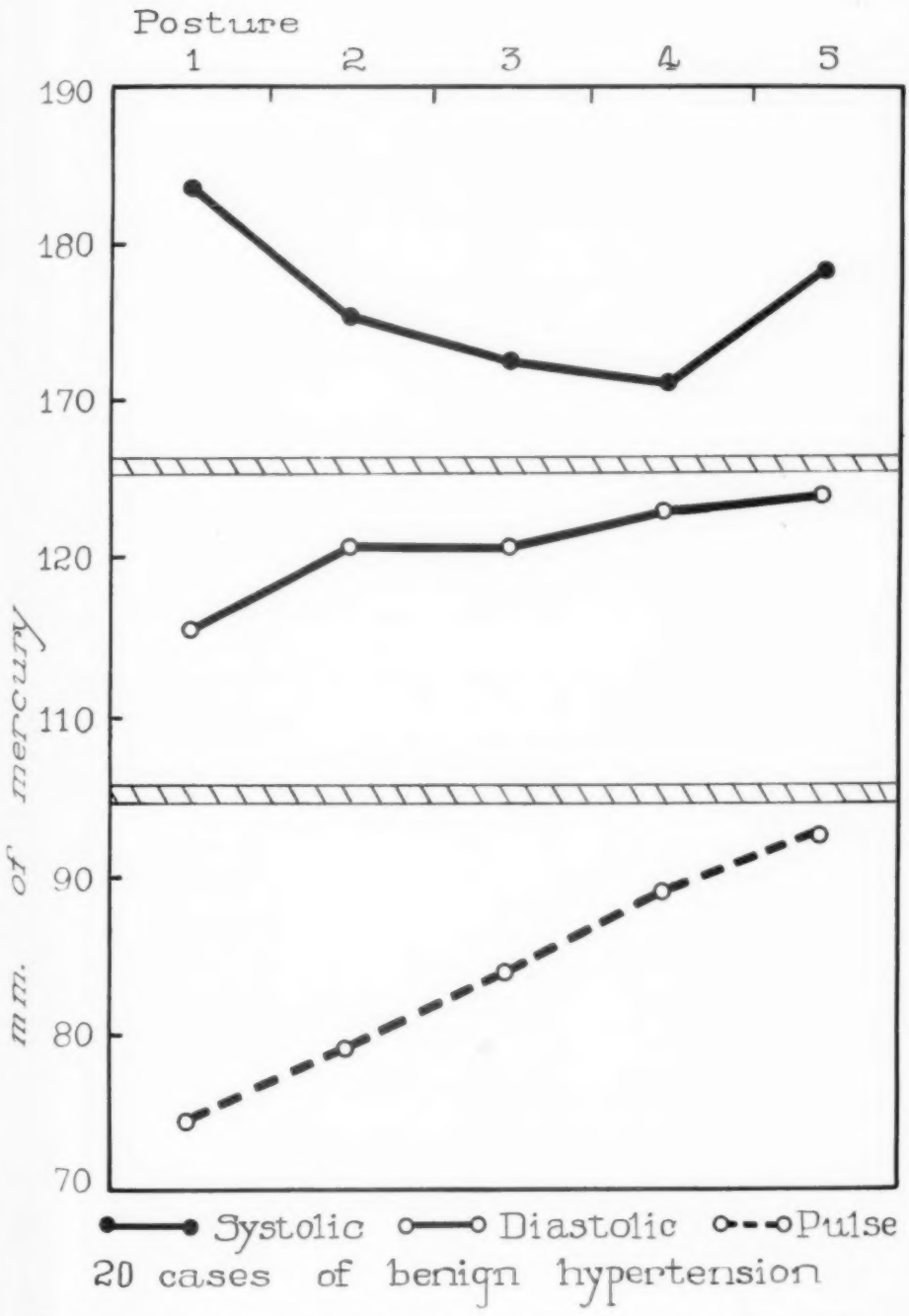

FIG. 2. Results of progressive change in posture of twenty patients with benign hypertension.

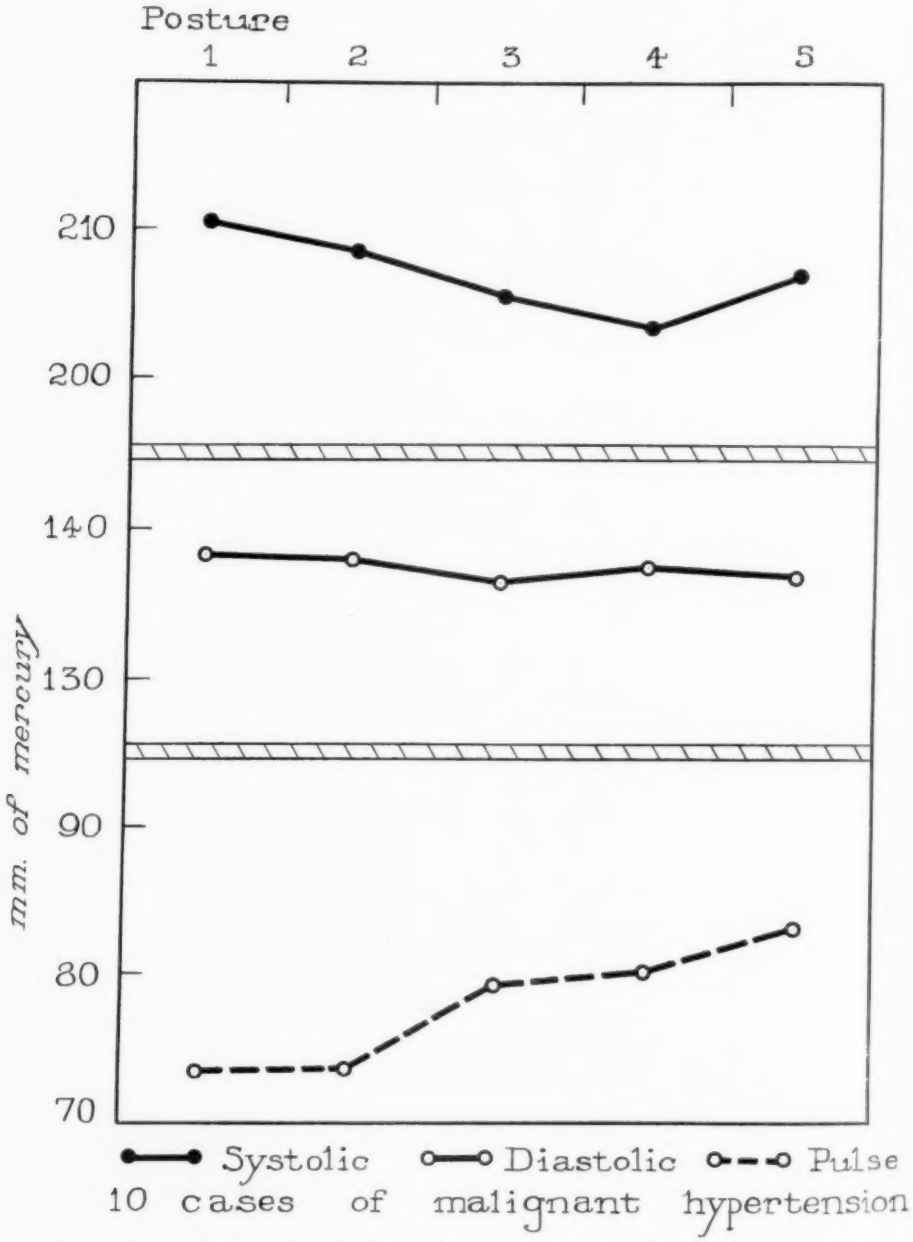

FIG. 3. Results of progressive change in posture of ten patients with malignant hypertension.

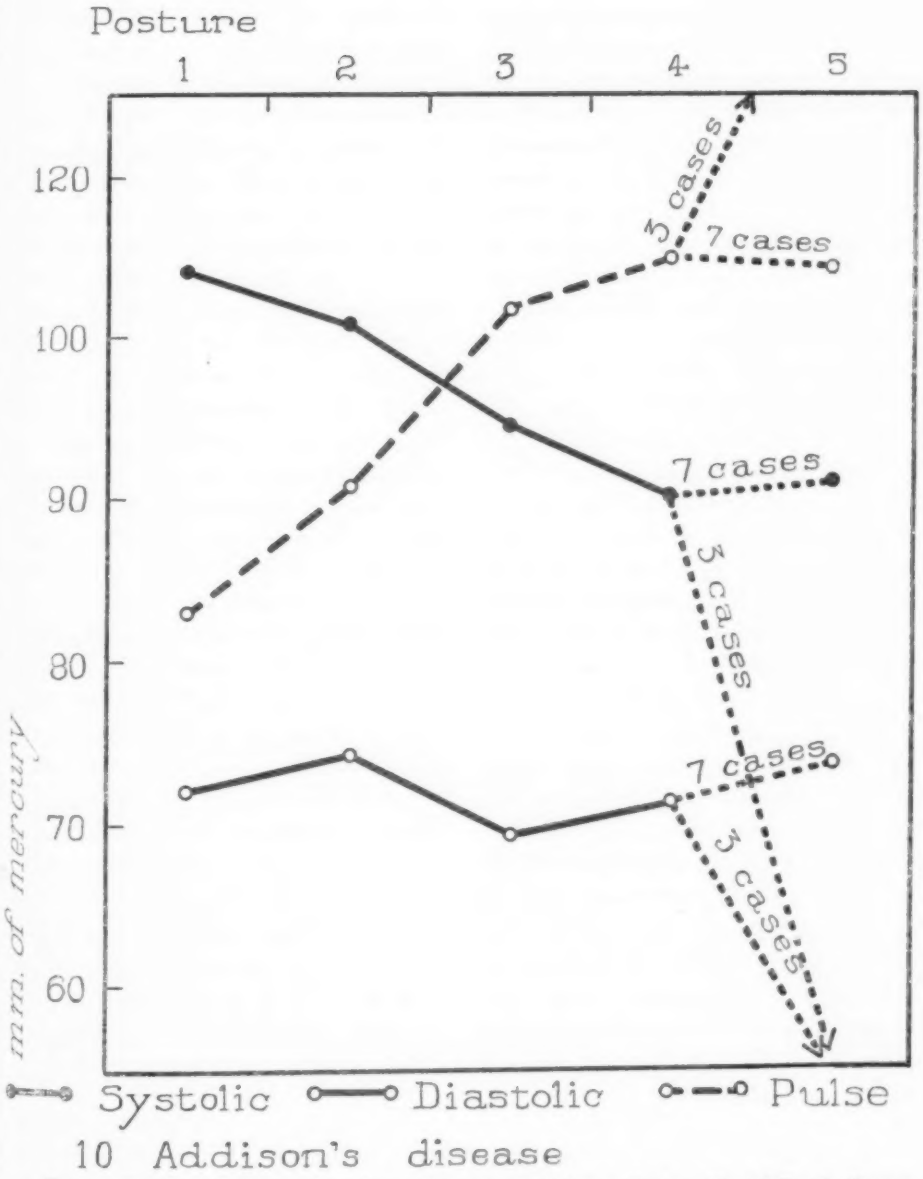

FIG. 4. Results of progressive change in posture of ten patients with Addison's disease.

In approximately 50 per cent of cases of diabetes mellitus, a history of weakness, dizziness or faintness on changing from a lying or sitting to a standing position can be elicited. Three of the thirteen patients with diabetes, who had a history of symptoms due to posture, exhibited these symptoms at posture 5 of the interrupted postural test. All patients with diabetes lacked stability in systolic blood pressure on postural test. Lack of normal vasopressor response also was seen in the group with diabetes. The explanation of this feature seems to lie in the factors of senile changes in the walls of the peripheral vessels; in the general weakness,† contributing to decrease of vasomotor tonus, and in the possible element of vasospasm present even under basal conditions. The senile arterial and arteriolar changes seem more important than either of the other possible factors of decreased vasomotor tonus in diabetic persons.

Of seventeen persons who did not have diabetes, but who were noticeably underweight and who had a history of symptoms of changing posture, five experienced weakness or dizziness at posture 5 in the interrupted postural test.† The postural reactions of these patients gave evidence of more marked deficiency in vasomotor tonus than those of other patients in the same group who were also deficient in vasomotor tonus. The systolic instability of these five patients outdid the same tendency in others of the same group. These observations give evidence that circulatory inefficiency on postural change was a definite factor in the postural symptoms of these patients.

In cases of weakness not associated with change of posture, symptoms were not produced by the postural test. This indicates that few complaints of general weakness are associated with significant circulatory deficiency on postural change unless a history of this relationship is elicited from the patient. This group gave evidence of normal activity of vasomotor tonus up to the last positions of the interrupted postural test; apparently, the interrupted type of test is of value in showing what evidently represents a fatigue element after three to four minutes of utilization of the vasomotor mechanism for postural adjustment. Inclusion of the pertinent cases of diabetes mellitus with the other cases in which there was a history of postural symptoms, brings out the fact that among these thirty-two patients, 25 per cent experienced weakness or faintness from undergoing the interrupted postural test*.

Conservative estimate of the incidence of severe circulatory embarrassment on interrupted postural change indicated that in 30 per cent of the ten patients with Addison's disease, the levels of systolic and diastolic blood pressure were approaching those of syncope when posture 5 was reached (tabulation and fig. 4). Two other patients (20 per cent) suffered definite

†The strength of more than 50 per cent of the patients who had diabetes mellitus was less than normal.

**A correlation of the presence or absence of anemia in all groups revealed no relationship between deficient circulatory response and anemia.

*Inclusion of Addison's disease and postural hypotension with syncope would appreciably raise the percentage incidence of symptoms during the postural test.

symptoms of circulatory embarrassment of posture 5. Fifty per cent of the patients either were under, or within thirty-six hours had been under the Muirhead regimen. Thus, the reactions of the patients should be taken conservatively in estimating the reactions of an untreated group of patients with Addison's disease. The striking failure of circulatory adjustment to posture which these persons exhibited, apparently arose from a combination of factors. Some of these factors were decreased size of the heart; failure of vasopressor adjustment, with shift of the mass of blood to the capillaries, venules and venous regions of the splanchnic circulation; general muscular weakness and atony which probably augmented inefficient venous return, and defective tonus of the walls of the blood vessels. Decrease or abnormality of circulating hormone from the suprarenal glands probably is a major factor in these abnormal reactions during passive postural change.

Subnormal vasopressor response to postural change, exhibited in cases of chronic infectious arthritis, corroborates previous work of myself in which decreased vasopressor reaction to stress and strain was exhibited by these patients. The rise of both systolic and diastolic blood pressure at posture 1, following performance of lumbar sympathetic ganglionectomy and trunk resection after the method of Adson, argues for compensatory augmentation of tonus in regions which have not been released from sympathetic control. The nonreleased splanchnic region of the patients who have undergone lumbar ganglionectomy and trunk resection continues to adjust as formerly, for postural change.

The two cases of Raynaud's disease exhibited little deviation from normal postural response except for instability of the systolic pressure, which might be expected. Cervicothoracic sympathetic ganglionectomy and trunk resection in these cases may slightly reduce the blood pressure in the region of the brachial artery by relaxing the vessels in the regions released from sympathetic control. The systolic instability shown preoperatively is absent postoperatively. No appreciable change in the reactions of diastolic blood pressure occurred following ganglionectomy and trunk resection.

The normal response of systolic blood pressure to postural change in four cases of scleroderma indicates stability of peripheral vascular resistance. Lack of vasopressor response, as indicated by relatively fixed diastolic pressure in all postures, seems best explained on the basis of vascular spasm, thickening of the vascular walls, and perivascular infiltration in the skin or surface areas. These conditions seem to be compensated for by relative relaxation of the splanchnic circulatory apparatus. Normal response to postural change in one of these cases following lumbar sympathetic ganglionectomy lends logic to this contention.

Correlation of the reactions to both interrupted and uninterrupted tests shows the following discrepancies in the results from the two types of passive change from the recumbent to the erect posture: slightly greater average fall of systolic and slightly greater average rise of diastolic blood pressure

obtains from the interrupted postural test, and slightly greater average rise of pulse rate obtains in the uninterrupted test. Since, in the interrupted test, approximately three minutes longer are available for circulatory adjustment than are available in the uninterrupted test, the readings at posture 5 in the interrupted test should give better qualitative and quantitative estimation of physiologic response than the uninterrupted test.

Summary and Conclusions

1. Fractional determinations of blood pressure, pulse, and symptoms, on passive change from recumbency to the erect posture, yield information as to pathologic physiology involving the circulatory apparatus in groups of cases in which disturbances of this type are suspected.

2. The incidence of normal response in many of the persons who comprise pathologic groups and vice versa make single determinations of little scientific value, except when the deficiency of circulatory adjustment is severe.

3. Neither hypotension nor undernourishment precludes normal response of the circulatory apparatus to passive change from recumbency to standing.

4. Patients with scleroderma, chronic infectious arthritis, and benign (essential) hypertension, taken as groups, exhibit subnormal rise of diastolic blood pressure on passive change from recumbency to standing, whereas patients with malignant (essential) hypertension taken as a group exhibit fixation of diastolic blood pressure during the same procedure.

5. The highest incidence of signs or symptoms of weakness, faintness or dizziness, on passive change from recumbency to standing, was found in groups of patients from whom a history of postural symptoms could be elicited.

6. Correlation, during the above postural tests, of inefficient circulatory adjustment, with the history of postural symptoms before the tests were performed, is possible in a certain proportion of cases.

7. Groups of patients diagnosed postural hypotension with syncope, Addison's disease, diabetes mellitus, and asthenia, present the highest percentage of correlation in the phenomena mentioned in the two previous sentences.

8. Patients with nonpostural weakness initiate normal circulatory adjustment to passive postural change but show evidence of fatigue in its maintenance.

9. Neither lumbar nor cervicothoracic sympathetic ganglionectomy and trunk resection appears appreciably to alter the manifestations of vasomotor tonus expressed by diastolic rise of blood pressure on change from recumbency to standing in cases of chronic infectious arthritis and Raynaud's disease.

10. Interrupted determination of postural adjustment by the circulatory mechanism yields results that can be seen in alterations of the same phenomena as those affected in the uninterrupted procedure, and, in addition, the interrupted method affords more qualitative and quantitative information.

GROUP STUDIES OF PULSE RATE BLOOD PRESSURE AND SYMPTOMS DURING PASSIVE POSTURAL CHANGE.

Group studied	Posture*	Average pulse rate	Average blood pressure: Systolic	Average blood pressure: Diastolic	Symptoms of dizziness, weakness or faintness	Average age, years	Average weight
Normal (23 women and 17 men)	1	72.6	118.5	72.3	Two women slightly faint at posture 5**	27.2	Approximately normal
	2	74.8	118.7	78.0			
	3	82.4	117.7	80.6			
	4	86.0	117.2	83.5			
	5	88.0	117.5	84.6			
Hypotension (systolic blood pressure 100 mm. or less) 11 cases	1	69.0	91.6	60.2	None	41.3	Underweight, 17 pounds
	2	74.9	91.8	61.5			
	3	78.4	92.2	66.2			
	4	83.4	91.8	67.9			
	5	87.8	91.3	70.0			
Benign (essential) hypertension, 20 cases	1	74.1	183.2	115.4	None	43	Overweight, 3.1 pounds
	2	79.0	175.0	120.3			
	3	83.9	172.1	120.6			
	4	88.8	170.8	122.7			
	5	92.1	177.8	123.4			
Malignant (essential) hypertension, 10 cases	1	73.2	210.4	138.2	None	44.6	Overweight, 1 pound
	2	73.7	208.8	138.0			
	3	79.3	205.4	136.6			
	4	80.1	203.4	137.4			
	5	83.2	207.0	136.0			
Generalized (senile) arteriosclerosis, 6 cases	1	78.6	150.0	89.0	None	59.3	Approximately normal
	2	81.5	147.0	91.6			
	3	84.8	144.5	90.0			
	4	91.0	142.8	95.3			
	5	94.7	147.0	96.6			
Postural hypotension and syncope, 1 case	1	84.0	128.0	98.0	Severe faintness and syncope at posture 5	41	Overweight, 5 pounds
	2	86.0	106.0	74.0			
	3	84.0	82.0	52.0			
	4	84.0	78.0	40.0			
	5	80.0	54.0	40.0			

Histories of postural symptoms before test *** 32 cases		1	80.3	124.4	82.4	Slight to moderate, 8 cases	44.2	Underweight, 5.4 pounds
		2	86.2	121.5	83.3			
		3	89.9	117.9	83.9			
		4	95.6	115.1	81.4			
		5	99.2	115.9	83.9			
Diabetes mellitus, 19 cases		1	83.6	129.9	82.5	Moderate, 3 cases	44.7	Underweight, 2 pounds
		2	86.9	127.7	83.1			
		3	92.2	125.8	85.4			
		4	97.0	122.4	87.9			
		5	101.0	125.8	87.0			
Nonpostural weakness, 15 cases		1	72.3	104.1	71.3	None	49.6	Underweight, 14.6 pounds
		2	77.5	104.0	75.6			
		3	83.6	101.7	78.3			
		4	87.2	101.7	78.3			
		5	93.3	102.9	76.9			
Addison's disease, 10 cases		1	83.0	104.0	72.0	Definite, 2 cases, severe, 3 cases	39.6	Underweight, 13.5 pounds
		2	91.6	100.8	74.2			
		3	101.6	94.4	69.2			
		4	Above 104.0	Below 90.0	Below 71.1			
		5	Above 104.0	Below 90.4	Below 73.5			
Chronic infectious arthritis, 9 cases		1	86.7	108.2	70.4	None	35.5	Approximately normal
		2	89.3	104.7	73.4			
		3	94.2	103.1	76.2			
		4	98.0	101.6	76.2			
		5	102.0	104.9	78.0			
Chronic infectious arthritis (5 of the 9 cases)	Before operation	1	93.7	103.7	66.8			
		2	96.0	102.6	71.5			
		3	100.4	103.4	72.0			
		4	109.0	100.0	73.4			
		5	108.6	108.2	77.3	None		
	After lumbar sympathetic ganglionectomy and trunk resection	1	92.8	108.4	70.8			
		2	99.2	105.2	75.2			
		3	112.8	104.8	72.0			
		4	118.0	104.8	76.8			
		5	122.0	109.2	81.6			

Group Studies of Pulse Rate Blood Pressure and Symptoms During Passive Postural Change—Continued

Group studied		Posture*	Average blood pressure				Average age, years	Average weight
			Average pulse rate	Systolic	Diastolic	Symptoms of dizziness, weakness or faintness		
Raynaud's disease, 2 cases	Before operation	1	78.0	118.0	75.0		29.5	Underweight, 18.5 pounds
		2	80.0	111.0	79.0			
		3	88.0	112.0	80.0			
		4	91.0	115.0	80.0			
		5	88.0	116.0	84.0	None		
	After cervicothoracic sympathetic ganglionectomy and trunk resection	1	88.0	112.0	69.0			
		2	88.0	111.0	71.0			
		3	92.0	111.0	77.0			
		4	96.0	110.0	81.0			
		5	96.0	113.0	76.0			
Scleroderma, 4 cases		1	80.0	113.5	72.5	None	36.2	Underweight, 26.5 pounds
		2	84.5	112.5	74.0			
		3	88.0	112.0	78.5			
		4	91.0	109.5	76.7			
		5	94.0	112.0	74.5			
Comparison of interrupted and uninterrupted methods, 32 cases	Interrupted method	1	76.1	127.2	83.1			
		5	90.7	125.0	91.8	None		
	Uninterrupted method	1	75.1	126.4	83.2			
		5	91.2	125.1	89.2			

* Posture 1 = 180° (horizontal)
Posture 2 = 157.5°
Posture 3 = 135°
Posture 4 = 112.5°
Posture 5 = 90° (erect)

** One of these had phobia for blood pressure determinations and the other was tested during menses.

*** Cases of Addison's disease and of postural hypotension with syncope excluded from this group, whereas thirteen cases of diabetes mellitus are included.

[1]Adson, A. W.: Surgical relief of Raynaud's disease and other vascular disturbances by sympathetic ganglionectomy and perivascular neurectomy. Ann. Clin. Med., 5:161-167 (Aug.) 1926.

[2]Ghrist, D. G.: The temperature of the upper and lower extremities in relation to the control exercised by the sympathetic nervous system. Proc. Staff Meetings of Mayo Clinic., 5:25-26 (Jan. 29) 1930.

[3]Ghrist, D. G. and Brown, G. E.: Postural hypotension with syncope; its successful treatment with ephedrine. Am. Jour. Med. Sc., 175:336-349 (March) 1928.

[4]Hill, Leonard and Barnard, Harold: The influence of the force of gravity on the circulation. Part II. Jour. Physiol., 21: 323-352 (May) 1897.

[5]Kernohan, J. W., Anderson, E. W. and Keith, N. M.: The arterioles in cases of hypertension. Arch. Int. Med., 44:395-423 (Sept.) 1929.

[6]Mortensen, M. A.: Blood-pressure reactions to passive postural changes: An index to myocardial efficiency. Am. Jour. Med. Sc., 165:667-675 (May) 1923.

[7]Schneider, E. C. and Truesdell, D.: A statistical study of pulse rate and the arterial blood pressures in recumbency, standing, and after a standard exercise. Am. Jour. Physiol., 61:429-474 (Aug.) 1922.

Venous Pressure in Pneumonia*

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In the study of the circulation in the normal individual, Eyster, Hooker, Clark and others have placed particular emphasis on the variations and importance of the venous pressure. The results of these investigations have given evidence that the venous pressure is altered greatly by varied demands on the circulatory mechanism. It has been observed that the venous return of blood to the heart apparently regulates in large part the arterial output. The venous pressure determines the degree of filling of the ventricular chambers in diastole, and this determines the amount of blood expelled at each contraction of the ventricles. An increased venous pressure, therefore, results in an increase in the amount of blood pumped into the arterial system. The normal heart responds to an increased venous pressure by increased output, and furthermore, is able to react favorably to great variations in pressure.

This physiological conception of venous pressure has been applied to the study of cardiac disease and especially in recent years its value as an aid in the clinic has been emphasized by Eyster and Middleton[1,2,3,4]. Eyster[4] (page 117) states that, "the condition in which the venous load exceeds the capacity of the heart to respond by increased output into the arterial system or in which the heart fails to move the blood adequately from the venous to the arterial side, is called cardiac decompensation or cardiac failure." Observations in cases of cardiac failure have shown that the increase of venous pressure is proportionate to the degree of cardiac failure, and may be used as a clinical guide of this condition. Venous pressure studies have been applied to the various types of organic heart disease and to conditions in which the heart is affected secondarily as a result of toxemia. From his clinical observations on venous pressure Eyster[4] (page 117) further states, "cardiac decompensation occurs only in the presence of heart muscle injury, either (and most frequently) as a result of degenerative processes superimposed on muscle hypertrophy, or as a result of toxemia (associated with pneumonia and more rarely other acute infections)."

Analysis of the few reported cases of lobar pneumonia with venous pressure observations indicates that in a small proportion of the cases the venous pressure was increased at some time during the infection. Schott,[5] in

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1912 reported 4 cases, all with normal venous pressure. Fuchs,[6] in 1929, reported 9 cases; 8 of this group maintained a normal venous pressure, with 2 fatal cases included. The remaining case had a normal venous pressure at the onset but developed signs of cardiac decompensation and an increase of venous pressure to 17.3 cm. on the third day. Venesection decreased this pressure to 13.5 cm. but the patient died on the fourth day. Eyster and Middleton,[1] in 1924 reported 8 cases. 6 of these had a normal venous pressure throughout the illness and showed no evidence of cardiac failure. 2 cases, with evidence of cardiac failure, showed a high venous pressure, one of which had two periods of increased pressure and ultimately recovered. These authors noted that a rising venous pressure and capillary stasis preceded the clinical evidence of cardiac failure.

We have had the opportunity of observing a number of cases of pneumonia in which venous pressure data have been collected. This report is composed of cases in the first two years of our work. The infection in this community is severe and has a subsequent high mortality. The cause of death in pneumonia has usually been attributed to cardiac or respiratory failure. We have been impressed from clinical observation with these possibilities but have been doubtful as to our ability to recognize signs of congestive heart failure in a patient seriously ill with pneumonia. We were therefore interested in venous pressure observations, particularly in the severe forms of the disease, and have been impressed by the value of these observations as an index of the state of the circulation. Further we have utilized venous pressure as a guide to intravenous dextrose medication in cases of pneumonia recently reported by us[10].

Materials and Methods

Ninety cases of pneumonia are reported as seen in hospital practice. We include under the term pneumonia the lobar and the bronchial forms; much of the infection in this community is of the latter type. Post-operative pneumonia and the infection in children are not included. The cases are divided into two groups to facilitate their study. Group "A" includes cases receiving the usual treatment for pneumonia, while Group "B" had intravenous dextrose therapy in addition.

The indirect method of determining venous pressure with the simple or compensating "U" tube water manometer was used, as described by Hooker and Eyster.[7] A portable instrument modified by one of us (Kastlin) was found to be most useful. An obsolete model of Faught "U" tube sphygmomanometer was converted into a venous pressure manometer by replacing the mercury with water. The two outlets of the manometer were used, one to the bulb, the other to the glass-top air chamber. The millimeter scale is adaptable to centimeters and is movable, to be readily adjusted to the fluid level in the tube which varies by evaporation, et cetera. The "U" tube instrument, in our experience, is easier to operate than the type with the tube and reservoir because of the ease of holding the compensated column of fluid steady while making the reading.

All readings were made by one of us and were made daily or oftener. The same prominent vein on the back of the hand was used in successive readings in each case. The patients were all recumbent and at rest, the vein held at cardiac level, which was taken as one-third of the distance from the anterior surface of the thorax to the dorsal surface at the level of the fourth intercostal space. The minimum pressure producing compression of the vein was accepted as the reading. Co-ordination between the hand holding the air chamber in contact with the skin and the hand applying pressure to the bulb is necessary to obtain consistent readings. Frequently the patient's hand must be shaved to obtain good vision of the vein. By perfection in technique, readings may be taken on small veins and on veins constricted by venomotor activity. In only one instance was observation impossible because of extreme thickness of the skin of the hands and over other peripheral veins. The above method insured uniform conditions for the taking of records as recommended by Eyster.

The normal venous pressure was considered to be any reading of 11 cm. of water or lower (Eyster and Middleton[1]). Cases with pressures of 12 cm. to 16 cm. were tabulated as slightly elevated. Elevation of 17 cm. or more of water was considered high or critical (Clark)[8].

DATA

Group A.. (Cases receiving usual treatment)
Total number..... 50
1. Normal venous pressure..... 28
2. Slightly elevated venous pressure... 9
3. High venous pressure..... 13

1. Cases with Normal Venous Pressure.. 28
Recovered 24
Died 4 (14%)

This chart would indicate that a large proportion of the cases showing a normal venous pressure recovered. A number of toxic cases were present in this group, indicating that a normal pressure is seen frequently in severe infection.

2. Cases with Slightly Elevated Venous Pressure 9
Recovered 8
Died 1 (11%)

The majority of patients with slight elevation of venous pressure recovered. This increase in pressure was constant throughout the illness except in one case in which the rise occurred just prior to the crisis. The normal reading was re-established at the time of crisis or towards the end of lysis in every recovered case. The fatal case, oddly, had a fall in venous pressure prior to death. Severe and mild cases were about equally divided.

3. Cases with High Venous Pressure.... 13
Recovered 5
Died 8 (61%)

This chart stresses the fact that the presence of a high venous pressure is associated with a high mortality. The high venous pressure was present at the time of our first observation in 8 of the cases, of which 4 recovered and 4 died. In the remaining 5 cases the venous pressure slowly increased from a normal to a high level during our observation, beginning on the third to the seventh day of the disease with one exception. In this instance a normal pressure was maintained throughout the illness, but on the day following a crisis-like reaction, the venous pressure rose

to 18 cm. and death occurred the next day. Once the pressure reached a high level it remained high for the remainder of the infection with readings fluctuating from 17 cm. to 22 cm., except in one instance in which there were two definite rises to 17 cm. with a normal venous pressure in the interval, during eleven days of illness. The duration of high pressure varied from one day to seven days before either crisis or death. All of the fatal cases in this group had a high venous pressure at the time of death.

In the recovered cases the pressure returned to normal at the time of crisis or towards the end of lysis in four instances. The fifth case was admitted in mild cardiac failure with auricular fibrillation. The high pressure had decreased from 21 cm. to 14 cm. at the end of lysis and remained at a 14 cm. to 16 cm. level throughout convalescence, although there were no unusual cardiac symptoms.

One case developed a reinfection in the opposite lung and the venous pressure again increased to a 16 cm. level and returned to normal at the second crisis. A temporary post critical rise to 17 cm. after a return of venous pressure to normal at the time of crisis, was noted in one patient. The rise in pressure was not associated with evidence of reinfection and the patient made an uneventful recovery.

Venesection was performed in three instances as a measure to reduce high venous pressure. It was done virtually in a terminal stage, a time when little benefit could be expected. In the first instance, venesection of 500 cc. reduced the pressure from 22 cm. to 10 cm. and there was marked temporary reduction in the cyanosis, and dyspnea, and improvement in the general appearance. Three hours later the pressure had increased to 15 cm. where it remained until death 6 hours after the venesection. In the second case, venesection of 400 cc. reduced the pressure from 17 cm. to 15 cm. but gave no clinical improvement. Within one hour the pressure rose to 20 cm. and death occurred. In the third case, venesection reduced the pressure from 20 cm. to 16 cm. There was no clinical improvement. Two hours later the pressure fell to 14 cm., moisture increased in the lungs and the patient died. These few examples indicate that an attempt to reduce venous pressure late in the toxic cases offers no therapeutic benefit and may also indicate that venesection in the terminal stages of pneumonia may even be dangerous.

Group B. Cases Receiving Intravenous Therapy

Early in our experience in the use of intravenous dextrose therapy in pneumonia, the solution was given in large amount and in low concentration (500 cc. of 5 to 10 per cent dextrose). During this early period no attempt was made to accurately determine the effect of a large amount of fluid on the circulation. Occasionally, however, the patients appeared clinically worse following the injections and showed evidence of circulatory embarassment.

When we first made observations on venous pressure in cases of pneumonia, we were able to show that although many cases maintained a normal venous pressure following the administra-

tion of 500 cc. of solution intravenously, in certain cases the venous pressure increased even to a critical level.

VENOUS PRESSURE RESPONSE TO INTRAVENOUS INJECTION

	Time	V. P.	Amount of Solution
Example I	7:25	11 cm. of H_2O	0
	7:30	12 cm. of H_2O	100 cc.
	7:35	13 cm. of H_2O	200 cc.
	7:45	14 cm. of H_2O	300 cc.
	7:55	15 cm. of H_2O	400 cc.
	8:00	15 cm. of H_2O	450 cc.
			Injection Stopped
Example II	4:30	14 cm. of H_2O	0
	4:50	16 cm. of H_2O	200 cc.
	4:55	17 cm. of H_2O	250 cc.
	5:00	18 cm. of H_2O	300 cc.
			Injection Stopped

This type of reaction clearly indicated that under certain conditions the intravenous administration of large amounts of solution may increase the venous pressure and, by overloading the right heart, induce circulatory embarassment in cases which otherwise might maintain a normal pressure.

To avoid the danger of large amounts of fluid, the amount of solution was decreased to 200 cc. of 25% dextrose. Administration of fluid in this volume and percentage of dextrose frequently resutled in a temporary increase in venous pressure of 1 to 2 cm. of H_2O. In cases with normal venous pressure there was often no increase in pressure. The introduction of hypertonic dextrose solution intravenously would be expected to increase blood volume by the attraction of fluid from the tissues into the vascular channels. Dr. J. H. L. Heintzelman[9] investigated this phase of our problem. His work, which will be published separately, shows that by our method of giving dextrose the blood volume is increased 19% and returns to normal within 40 minutes. This temporary increase in blood volume apparently produced the temporary slight increase in venous pressure. We believe that in the presence of normal or only slightly elevated venous pressure such a slight and temporary rise is of no consequence, provided the myocardial tone be adequate.

The routine procedure established by our experience in the present series was as follows: 200 cc. of 25 per cent dextrose solution was the maximum amount of solution to be given at one time. The fluid was given slowly and not more frequently than once each fourth hour. Routine venous pressure readings were made daily. In the presence of an elevated venous pressure more frequent readings were made. If the pressure increased above the temporary fluctuation we reduced the amount of the fluid volume injected to 100 cc., and when a persistent high venous pressure developed the procedure was discontinued. Repeated small injections were frequently well tolerat-

ed, in the presence of elevated pressure. Cases admitted with an established high venous pressure received no intravenous therapy.

In the following cases intravenous injections were given from one to six times per day over a period of from 3 to 14 days.

Total Number of Cases..... 40
1. Normal Venous Pressure..... 9
2. Slightly Elevated 10
3. High Venous Pressure..... 21

1. Cases with Normal Venous Pressure.. 9
Recovered 8
Died 1 (11%)

The mortality of this group is low and compares with the normal group under the usual treatment.

2. Cases with Slightly Elevated Venous Pressure 10
Recovered Venous Pressure 4
Died 6 (60%)

The mortality shown by this chart is much higher than the corresponding cases in Group A. This may be explained by the fact that the cases were more toxic. As in the corresponding cases the slight elevation was present throughout the illness in the majority (8), and appeared late in the disease in the remainder (2). Also each of the recovered cases showed a return to normal pressure at the time of crisis, and all of the fatal cases had a slight elevation of pressure at death. Intensive administration of 200 cc. of dextrose solution intravenously resulted in only the temporary fluctuation of 1-2 cm. in venous pressure with the following exceptions. In one case the venous pressure varied from 11 cm. to 15 cm. during the course of disease after injections and in another there was a slight elevation just before crisis. Both of these cases recovered. Also, in one fatal case, the administration of only 100 cc. of fluid early in the infection produced a 7 cm. elevation in pressure, and further intravenous medication was not attempted. In another case, on the contrary, the pressure fell slightly after each injection. This last observation is worthy of note.

3. Cases with High Venous Pressure.. 21
Recovered 5
Died 16 (77%)

The highest mortality is seen in this group. Clinically they represented the most toxic cases and for that reason were given intravenous therapy. A normal venous pressure at onset was seen in all of the recovered cases and eleven fatal cases. The pressure in these cases increased late in the disease, the 5th to 10th day, and each case had a high venous pressure at crisis or death. Intravenous injections were well tolerated and changes other than the temporary fluctuations were not noted early in the infection, except on two occasions. In the first, following an initial injection of 200 cc. the venous pressure was raised from normal to 18 cm. It fell spontaneously illustrating a good cardiac reserve but further injection was not attempted. The second showed slight rises after each injection which quickly returned to the former level, but on two occasions rose to 18 cm. Intravenous injection was discontinued at the critical level but was resumed when a lower level was reached. Both of these cases recovered.

The general trend of development of high venous pressure and return to normal in recovery was the same in this group as in the corresponding

group under usual treatment. It is our belief that with the above routine venous pressure observations the venous pressure was not unduly influenced by intravenous medication save in the exceptions noted.

Venesection was performed in 9 cases of this group with the hope of reducing venous pressure so that intravenous injections of small amounts of fluid could be continued. In three cases a venesection of 100 cc. was done preceding an intravenous injection of the same amount. In each instance the pressure was reduced slightly by venesection and returned to the previous level after intravenous. This produced no demonstrable benefit. In 6 cases a venesection of from 350 to 400 cc. was performed preceding an intravenous injection of 75 to 100 cc. Of these, three were done from the third to fifth day of disease and the venous pressure was permanently reduced from levels of 18 and 19 cm. to 14 cm., and the cases recovered. The remaining three cases were done virtually as terminal procedures. The venous pressure was reduced from levels of 18 and 22 cm. to 12 and 14 cm. respectively, and death occurred within 24 hours. Repetition of venesection was done once, following a return of high pressure 24 hours after the first procedure. The pressure was again reduced but death came soon afterward.

Discussion

The clinical signs of failing circulation which are so obvious in primary heart disease do not appear or are interpreted with difficulty in pneumonia, particularly in severe or toxic cases. They are partially masked by the physical signs of the consolidated lung or by complications common in pneumonia. Dyspnea, cyanosis, and pulmonary moisture may all be due to lung disease. Palpation of an enlarged liver is often rendered impossible by abdominal distension. Edema of the limbs rarely is noted.

In the tabulation of total cases (table A) it will be seen that the proportion of cases showing clinical signs of circulatory failure is small compared with the proportion of cases with elevation in venous pressure. Although Eyster[4] has stated that, "circulatory failure in an acute infection like pneu-

TABLE A

	Cases	V. P.	Signs of Cir. Failure	
90 cases	37 (41%)	Normal	Cyanosis	7
			Vascular tonus changes	2
	19 (21%)	Sl. Elevated	Edema of ankles	2
			(1 with old cardiac disease)	
			Cyanosis	6
	34 (37.7%)	High	Cyanosis	All
			Positive centrifugal venous pulse	1
			Vasomotor changes	2
			Icterus	3
			Enlarged liver	2
			Edema	1
			Valve disease, Plus edema	1

monia does not appear to differ in any essential details from the same condition developing in primary heart disease," the infrequent appearance of the cardinal signs in pneumonia may be due to the relatively short duration of circulatory embarrassment. This is especially significant in that two of the four cases with edema were cases with old organic heart disease. If venous pressure is of value in estimating the circulatory state in primary heart disease it appears to be of an even greater clinical use in pneumonia where the usual pathognomonic signs are of so little value.

Blood pressure and pulse rate have been used as guides of severity of pneumonic cases and these criteria have been used as prognostic signs. It has been declared by various writers that a low or decreasing blood pressure is evidence of failing circulation in pneumonia. It is known that whereas venous pressure bears a direct relationship to cardiac efficiency, it bears no constant relationship to blood pressure. Blood pressure records were made on 70 cases. Table B illustrates the number of cases of high, average, and low blood pressure occurring in the presence of normal, slightly elevated, and high venous pressure. It will be seen that 71.4 per cent of the cases had an average blood pressure, 11.4 per cent had high and 17.1 per cent had low blood pressure.

It is interesting that the majority of cases with low blood pressure occurred with a normal venous pressure, and the great majority recovered. The highest mortality comes in the average blood pressure group with increased venous pressure. A high blood pressure appears to have a greater mortality significance than low pressure in this small series.

The pulse rate has been, in our experience, a valuable index of severity or toxicity in pneumonia. An elevation in rate to 120 per minute or greater was considered evidence of severity. We were thus particularly interested to check venous pressure records with the pulse rate. Table C presents this data for the 90 cases.

It will be seen that in the group with normal venous pressure the majority of cases had low pulse rates, in the slightly elevated group the proportion is about equal, while in the high venous pressure group the majority have a high pulse rate. The general mortality for cases with high pulse rate is 63.6% and low pulse rate 19.1%, for a practically equal num-

TABLE B

Venous Pressure	Blood Pressure					
	High		Average		Low	
	Lived	Died	Lived	Died	Lived	Died
Normal	3	1	19	2	7	1
Slightly Elevated	1	1	5	4	2	0
High	1	1	5	15	1	1
Total	5	3	29	21	10	2
	Mort. 37.5%		Mort. 42%		Mort. 16.6%	

TABLE C

Venous Pressure	Pulse Rate					
	Above 120			*Below* 120		
	Lived	Died	Mort.	Lived	Died	Mort.
Normal	9	2	18%	23	3	11.5%
Slightly Elevated ...	3	5	62.5%	9	2	18%
High	4	21	87.5%	6	4	40%

ber of cases. From the data presented previously there is also a definite correlation between degree of venous pressure and mortality. The mortality in normal venous pressure cases is 13.5%; in slightly elevated pressure 36%; and in high pressure 70%. Comparing these mortality figures with the pulse rate mortality figures it will be seen that in each venous pressure group the mortality in cases with pulse rate above 120 is greater than in cases below 120. The lowest mortality occurs with normal venous pressure and slow pulse rate; the highest mortality with high venous pressure and rapid pulse rate.

From our experience we believe that a rising venous pressure is the earliest method of recognizing circulatory failure in pneumonia. Used in conjunction with other clinical phases of the disease we feel that these observations have been to us of considerable bedside value.

Venous pressure observations form a basis for measuring the circulatory condition of the patient at the time the reading is made. A single reading is of relatively little value. Repeated readings offer a graphic record of the trend of circulatory state. They are not a means of predicting the outcome of the case, for the outcome depends on the ability of the heart to withstand the added work. For example, a case running a normal course may suddenly develop failure, and on the contrary, a case with a persistently high venous pressure may recover if sufficient reserve is maintained. However, venous hypertension has some prognostic value, in that, we know such changes are associated with a high mortality. A progressively rising venous pressure, particularly late in the infection, is most significant of a bad prognosis.

Sudden fluctuations are not uncommon but in general the development of a high venous pressure extends over a period of a few days. The three cases developing sudden increase of venous pressure after crisis seem of particular significance. The mechanism of such a reaction is difficult to explain but it points out that sudden changes after crisis may be due to acute circulatory failure which may be fatal.

We do not disregard the fact that death in pneumonia is also induced by causes other than circulatory failure. This is shown by fatal cases which have maintained a normal venous pressure throughout the disease. Because of the high incidence of circulatory failure in pneumonia and its definite relationship to mortality, every patient during treatment must be considered a potential case of circulatory failure.

The method of intravenous hypertonic dextrose treatment used in this series, we believe, added no additional risk to the circulatory apparatus when guided by venous pressure records.

The use of venesection in toxic and infectious states involves different problems than in primary heart disease, where a purely mechanical problem is at hand. Relief of early high venous pressure by venesection may be of benefit, as shown by three cases. At this period mechanical relief by venesection may allow a heart with good reserve to gain a permanent advantage. As disease progresses, the effect of toxemia and anemia decreases a possible therapeutic value and late in the disease venesection may even be dangerous.

Conclusions

1. Observations on the estimation of venous pressure by the indirect method (Eyster and Hooker) have been made on a series of cases of pneumonia.

2. An increase of venous pressure is evidence of circulatory failure in pneumonia.

3. The estimation of venous pressure is of particular value in recognizing circulatory failure in pneumonia, because the usual signs of congestive heart failure are difficult to recognize in this disease.

4. The correlation of venous pressure and pulse rate offers the best means of estimating circulatory failure in pneumonia.

5. The presence of increased venous pressure is associated with an increased mortality in pneumonia.

6. Venous pressure estimations are of value in controlling intravenous therapy in pneumonia.

7. Venesection is controlled by venous pressure determinations; and under certain early conditions may be of value, but in general, late in the pneumonic infection is of little therapeutic worth.

BIBLIOGRAPHY

[1]Eyster, J. A. E. & Middleton, W. S.: Clinical Studies of Venous Pressure. Arch. Int. Med., 34:228, 1924.

[2]Eyster, J. A. E. & Middleton, W. S.: Venous Pressure as a Guide to Venesection in Congestive Heart Failure. Am. J. M. Sc., 174:486, 1927.

[3]Eyster, J. A. E.: Venous Pressure in Cardiac Decompensation. J. A.M. A., 89: 428, 1927.

[4]Eyster, J. A. E.: "Clinical Aspects of Venous Pressure." The Macmillan Co. N. Y. 1929.

Venous Pressure." The Macmillan Co., as a Method of Functional Measurement of Heart in the Human. Deut. Arch. f. kl. Med., 108,537, 1912.

[6]Fuchs, Ludwig: Measurement of Venous Pressure and Its Clinical Significance. Deut. Arch. f. kl. Med., 134-35.68, 1920-21.

[7]Hooker, D. R. & Eyster, J. A. E.: An Instrument for the Determination of Venous Pressure in Man. John-Hop. Hos. Bull., 19:274, 1908.

[8]Clark, A. H.: Study of Diagnostic and Prognostic Significance of Venous Pressure Observations in Cardiac Disease. Arch. Int. Med., 16:587, 1915.

[9]Heintzelman, J. H. L.: To be published.

[10]Maclachlan, W. W. G., Kastlin, G. J., Lynch, R.: The Use of Dextrose in Pneumonia. Am. J. M. Sc., 179:93, 1930.

Acute Coronary Occlusion
A Clinical and Electrocardiographic Study of Twenty Cases

By Louis H. Sigler, M.D., *Brooklyn, N. Y.*

ALTHOUGH the pathologic changes associating embolic, thrombotic and endarteritic occlusion of the coronary arteries have been fully described for many years, the clinical picture resulting from such changes seems to have come into prominence only recently. As late as 1906, Broadbent stated that "there are no characteristic physical signs or symptoms by which thrombosis of the coronary arteries can be diagnosed." Blumer, in the 1915 Edition of Osler and McCrae's "Modern Medicine" stated that the symptoms of this condition are "not very characteristic and it is only rarely that the lesion can be diagnosed during life . . . . . The diagnosis of coronary artery thrombosis or embolism is at best a question of probabilities." The same view was held by Price in 1918 who stated that "complete and abrupt closure of a coronary artery is usually fatal. If the vessel is small, the patient may recover, but the condition is one which is recognized with difficulty during life."

These views have changed in recent years. Due to a greater prevalence of arteriosclerotic heart disease and to the refinement in the differential diagnosis of the various forms of such disease, we came to recognize a definite clinical syndrome, pathognomomic of coronary occlusion. Concomitant with the clinical syndrome, certain pathognomonic electrocardiographic changes have been observed and have come to be considered characteristic of the disease. Furthermore, we now realize that the disease is usually not immediately fatal, and including the milder forms of occlusion, is rather prevalent and has a favorable prognosis.

Although the clinical syndrome has been repeatedly described, the association of its various manifestations with the anatomico-physiologic changes taking place in the heart have not been stressed. This paper is an attempt to do so, and to bring out certain important factors in the elctrocardiographic study of such cases. The paper is based on a study of twenty cases in various phases of the disease.

Case Reports

Case I. A. S., female, housewife, 58 years old, was suffering from a mild form of diabetes and hypertension for fifteen years. While at perfect rest, she was suddenly seized, one day, with excruciating pain in the substernal region radiating to the left shoulder, together with vomiting, dizziness and a sensation of impending dissolution. I saw her eighteen hours after the onset of symp-

toms at which time I found her to be markedly dyspneic, her color was ashen, and a cold perspiration covered her body. Her lungs showed numerous râles at the bases posteriorly. The heart was enlarged to the left and right, sounds were almost inaudible, rate was about 120, rhythm regular. The blood pressure was systolic 100, diastolic 80. The liver was enlarged and tender.

The next few days she seemed to be heading towards recovery. The pain subsided. The temperature came down from 101 F. on the second day to normal on the fourth day. Eight days after the onset, however, she suddenly developed severe pain in the left lower chest together with dyspnea, cough and bloody expectoration. There was evidence of infarction of the lower lobe of the left lung the following day, with signs of onset of pulmonary edema. She died three days later.

The electrocardiographic tracing (Fig. 1) taken ten days after the onset, showed a simple tachycardia with delayed P-R conduction time, about .23 second, and a low S-T take-off in Leads 1 and 2. There was a tendency towards left axis deviation.

Case II. M. E., female, 66 years old, domestic help, was suddenly seized, about one-half hour after breakfast, with severe epigastric pain, vomiting and collapse. The condition was relieved after three hours by morphine. The next day, her temperature was 100 F., pulse 110, very irregular, and respirations 25. The leucocyte count was 14,200. The heart sounds were muffled, and a definite gallop rhythm was present. There was marked peripheral arteriosclerosis.

The electrocardiogram, four days after the onset (Fig. 2), showed a marked sinus arrhythmia, left axis deviation, slurring of the S wave in the first lead and notching of QRS in the third lead, depression of the S-T segment in first lead, and elevation and rounding of the R-T segment in the second and third leads, with markedly negative T waves in those leads. About two weeks later (Fig. 3), the S-T segment in the first lead was on the isoelectric level, while the T waves in the second and third leads were more markedly negative. The S wave in the first lead and the R wave in the third lead were of much smaller amplitude.

Three weeks after the onset she felt quite well and insisted upon resuming her work. I am informed that she is living and feels quite well at present, two years after the attack.

Case III. J. K., male, 77 years old, retired merchant, with a negative past history, was suddenly seized with excruciating pain in the region of both breasts, radiating to the left arm, left leg and to the back. It lasted several hours and was only partially relieved by morphine. He had had a similar but milder attack three months before, lasting ten minutes, which was considered to be a form of indigestion, as it was relieved by belching. I saw him twenty hours after the onset of the second attack at which time he was ashen in appearance, respirations were rapid, and his body was covered with a cold, clammy perspiration. He had marked peripheral arteriosclerosis. The heart was of normal size, sounds hardly audible, with a total irregularity, the ventricular rate being 120 and pulse rate 90. The pulse could hardly be felt. The liver extended about four inches below the costal margin, and was tender.

The next day he showed definite signs of pulmonary infarction. His temperature was 101 F., ventricular rate about 139 and pulse rate 104. The electrocardiogram (Fig. 4) showed auricular fibrillation and slurring of the QRS complexes in all leads. The T wave changes were not distinctly discernible, due to the fibrillation, but they seemed to be negative.

His subsequent course was rapidly downward. He had three more attacks of precordial pain during the following three months, and died about four months after the onset.

Case IV. B. M., female, 55 years old, with a history of hypertension of several years standing, and occasional precordial pain coming on after exertion for the past year, suddenly developed excruciating retrosternal pain, radiating to the throat, and associated with a sense of strangulation. The pain appeared while the patient was at per-

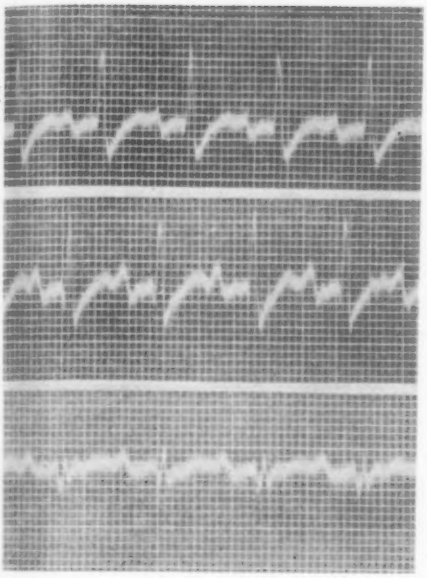

FIG. 1

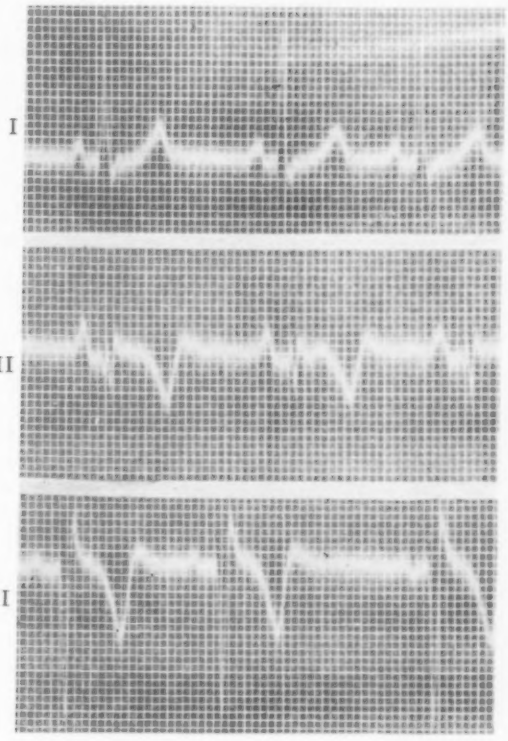

FIG. 3

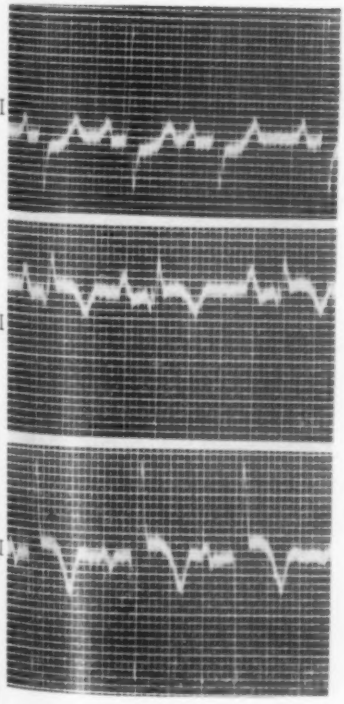

FIG. 2

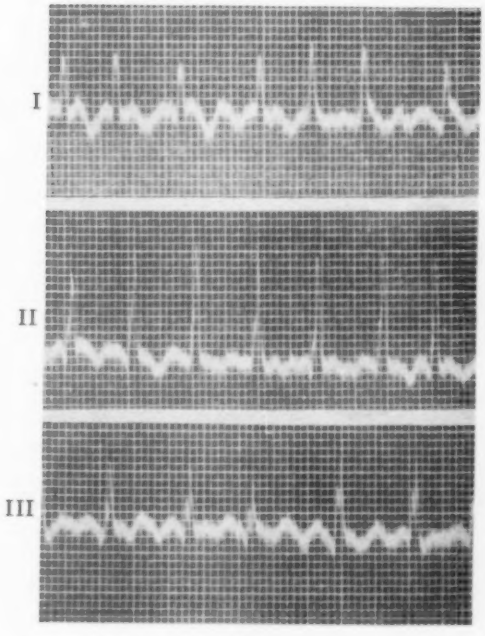

FIG. 4

fect rest, after a mid-day meal, and lasted two hours.

I saw her one week after the onset, when she showed slight cyanosis, and marked dyspnea. Her heart was enlarged to the left, sounds distant, almost inaudible, rate 105, rhythm regular. There was moderate peripheral arteriosclerosis. The blood pressure was systolic 150 and diastolic 115.

The electrocardiogram (Fig. 5) showed left axis deviation, slurring of the S and R waves in the first and third leads and notching of the S wave in the second lead, delayed QRS conduction time to .12 of a second, the S-T and R-T segments in all leads were above the isoelectric line, and there was a negative T wave in the third lead.

She is still alive, 15 months after the attack.

Case V. R. K., female, 61 year old, with a history of hypertension of ten years standing, was suddenly seized with excruciating midsternal pressure and pain, radiating to the left arm, associated with a sensation of fainting, coldness of the whole body, and marked sweating. The pain lasted about ten hours. I saw her at the end of four weeks, when she appeared pale and markedly irritable. Her heart was enlarged to the left, and sounds were muffled. The lungs showed numerous basal râles. The blood pressure was systolic 150, diastolic 110.

The electrocardiogram (Fig. 6), showed left axis deviation, rounding of the S-T segment in the second lead, high R-T take-off in the third lead, markedly negative T wave in the second and third leads, especially in the latter, and increase in the height of the T wave in the first lead.

I saw her four months later at which time her heart sounds were found to be markedly improved, and her blood pressure was systolic 210 and diastolic 130. An electrocardiogram taken at this time (Fig. 7), did not show any definite left axis deviation, and the T wave in the second and third leads was less negative. Eight months later, the electrocardiogram (Fig. 8) showed a negative T wave only in the third lead. Physically she was found to be greatly improved, but was subject to repeated precordial pain.

Case VI. A. C., male, 38 years old, dentist, never had any symptoms of heart disease. He smoked considerably all his life and was subject to attacks of angioneurotic edema. While sitting at rest one day, he suddenly felt a very severe "tightening" in the center of the sternum which lasted fifteen minutes and subsided, leaving him with no other ill effects than an apprehension of its return. Two days later, he got a second and far more severe attack lasting several hours and requiring large doses of morphine to give partial relief. This attack was associated with a sensation of fainting and a feeling of imminent death. His whole body was covered with a cold perspiration. The following day he felt quite comfortable. I saw him at my office three days after the second attack when his heart was of normal size and shape, sounds of fair quality, rate 72, rhythm regular. The peripheral vessels were slightly thickened. The electrocardiogram (Fig. 9) showed left axis deviation, rounding and slight elevation of the R-T segment in the first lead, slightly negative T wave in the second lead and markedly negative T wave in the third lead.

I saw him again ten weeks later and found his condition to be the same as before. Aside from a dull precordial ache, he had no complaints. The electrocardiogram (Fig. 10) then showed a definitely negative T wave in the second and third leads with slight depression of the R-T segments in those leads.

Case VII. J. T., male, 51 years old, with a history of hypertension for several years was suddenly seized, after his evening meal, with a severe sense of "tightness" in the precordium and epigastrium, radiating to both arms. This was associated with collapse and cold perspiration. Large doses of morphine gave relief after three hours. I saw him about four hours after the onset when he appeared to be quite comfortable. He was markedly obese and slightly cyanotic. His heart was enlarged to the left, sounds were of poor quality and rhythm regular. The blood pressure was systolic 120 and dia-

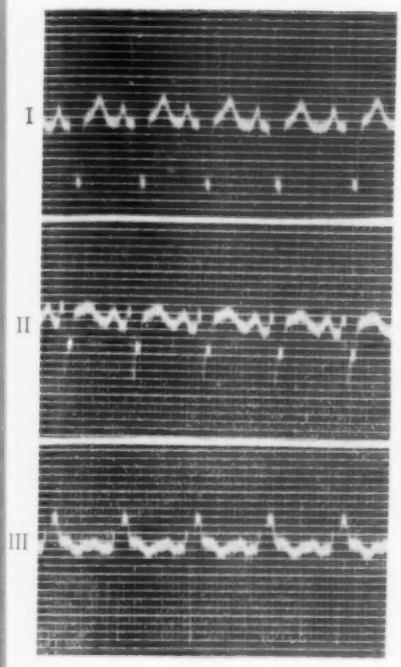

FIG. 5

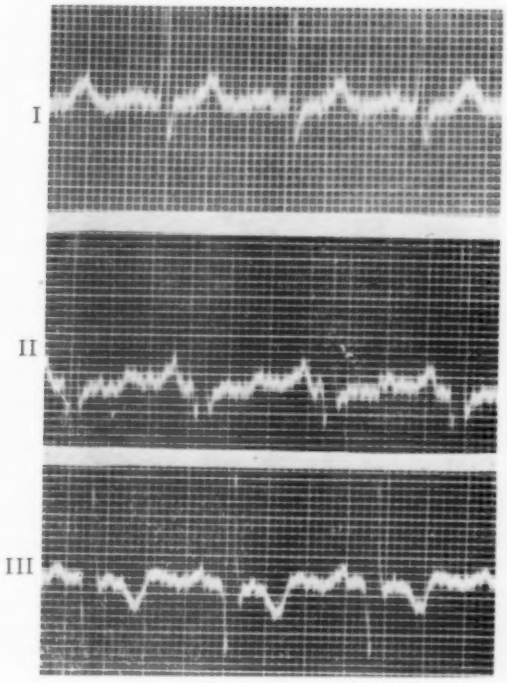

FIG. 7

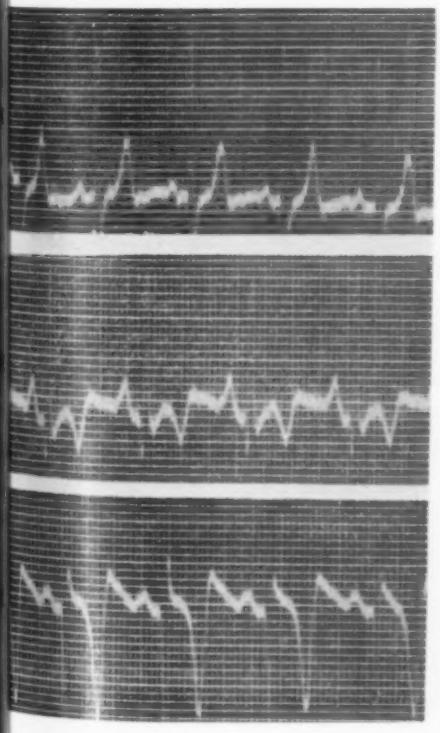

FIG. 6

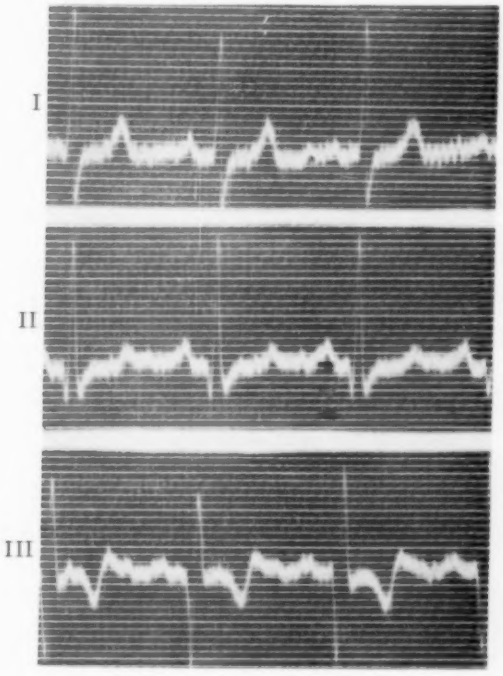

FIG. 8

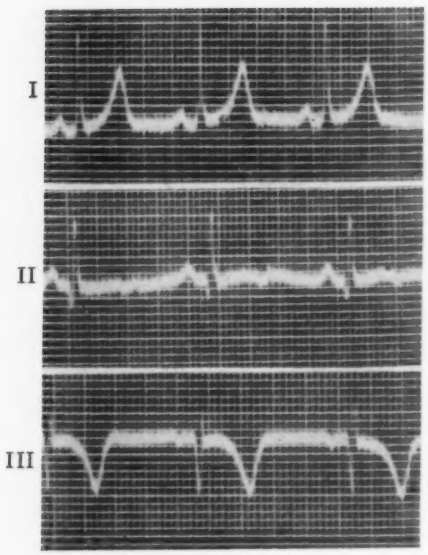

FIG. 9

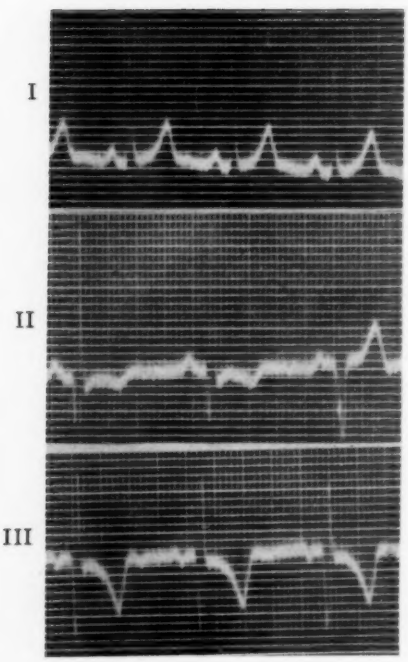

FIG. 10

stolic 80. The lungs showed numerous basal râles. The peripheral vessels were markedly sclerotic. The next day his temperature was 101 F., pulse 72, and blood pressure was systolic 110, diastolic 80.

The electrocardiogram (Fig. 11) showed left axis deviation; notching of the R wave in the second lead, rounding and elevation of the R-T segment, with a markedly negative T wave in the second and third leads.

At present, 10 months after the attack, he feels well and does considerable work with comfort.

Case VIII.—M. T., male, 50 years old, laborer, was always a hard worker and had never had any symptoms indicative of heart disease. Aside from a severe attack of influenza eight years ago, and considerable use of tobacco, his history is essentially negative.

While working, one morning, he was suddenly seized with severe precordial pain and oppression lasting four hours. No untoward effects apparently followed this attack, as he resumed his work two days later without discomfort. Six months later, he had a more severe attack of a similar nature, associated with collapse. Three-fourths grain of morphine were necessary to give relief. This attack lasted 24 hours. Since then he has experienced shortness of breath and dull precordial pain on any moderate exertion.

I saw him three weeks after the second attack when he presented a normal sized heart. The first sound was muffled and split. The peripheral vessels were markedly sclerotic, pulse weak, and blood pressure was systolic 120, diastolic 95. The electrocardiogram (Fig. 12) showed rounding of the R-T segment and a markedly negative T wave in the second and third leads.

Case IX.—M. H., male, 62 years old, merchant was suddenly seized with excruciating pain in the epigastrium, radiating behind the sternum to the left shoulder, together with belching, cold perspiration, vomiting and a sense of suffocation. He was partially relieved by morphine after several hours. This was followed for many weeks by dull precordial pain, palpitation, marked mental depression, dyspnea and great weakness. There was a rise in temperature for two weeks

following the onset, ranging between 100 and 101½ F.

Examination one week after the onset, showed his heart to be of normal size, the first sound muffled, and an occasional pericardial friction rub was audible at the apex. The pulse was very weak, and the blood pressure was systolic 100 and diastolic 70. These findings were practically the same throughout the course of his illness, lasting about four months, except that the pericardial friction rub disappeared after two days, and a presystolic gallop rhythm appeared two months later. He died suddenly, while sitting up in a chair.

Four electrocardiograms in his case are reproduced. The first one (Fig. 13) was done about one month after the onset and showed left axis deviation, isoelectric T wave in the second lead, rounding of the S-T segment and negative T wave in the third lead. Five weeks later (Fig. 14), the left axis deviation was not marked, and the second and third leads showed a negative T wave. Four weeks later the tracing (Fig. 15) showed absence of left axis deviation. Still later the electrocardiogram (Fig. 16) showed a tendency towards right axis deviation, and the T wave in the second and third leads was not so deep.

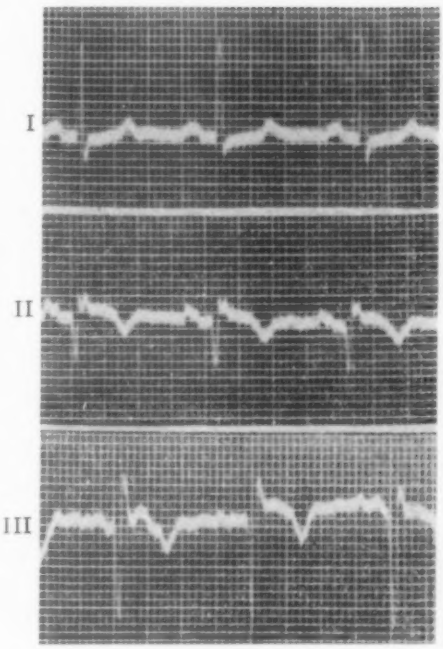

FIG. 11

Case X.—W. B. C., male, 58 years old, bank guard, was a heavy smoker all his life, had pleuro-pneumonia at 23 years of age, was subject to frequent colds, and had hypertension for several years. Coming home from work one day, he was suddenly seized with severe pain in the epigastrium radiating to the retrosternal region and to the back, with fainting and cold perspiration. The pain lasted four hours and was relieved by morphine. Since then he was subject to exertion dyspnea and dull precordial pain.

I saw him eight months after the attack, when he presented marked obesity and considerable peripheral arteriosclerosis. His face had a slight cyanotic flush. His tonsils were hypertrophied and diseased. The lungs were emphysematous and numerous inspiratory râles were heard over the bases. The heart was markedly enlarged, first sound weak, rate 96, rhythm regular. The blood pressure was systolic 158, diastolic 100.

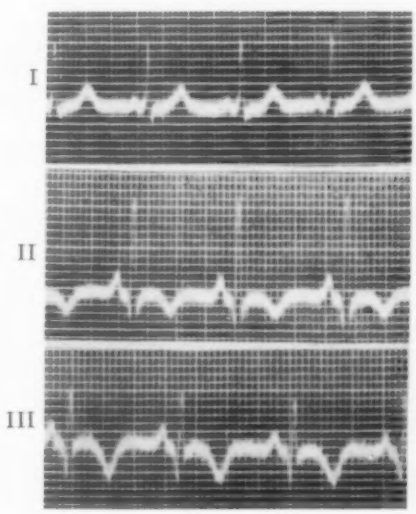

FIG. 12

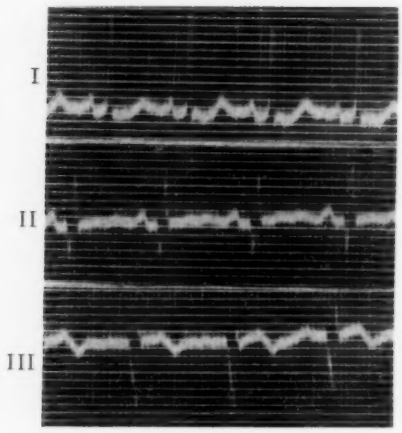

FIG. 13

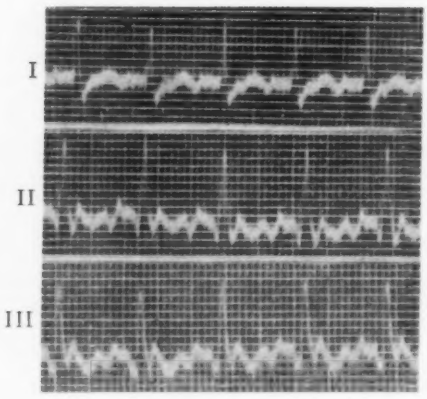

FIG. 15

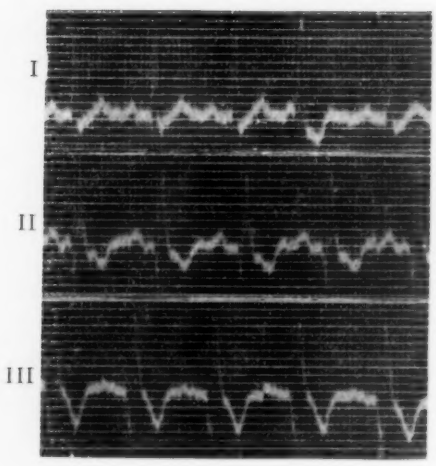

FIG. 14

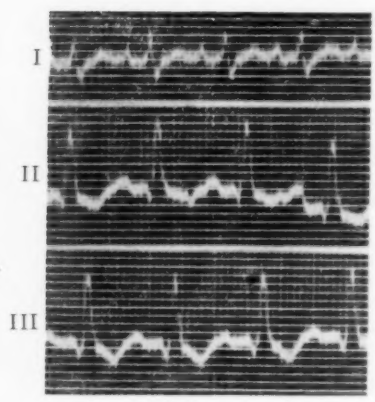

FIG. 16

The electrocardiogram (Fig. 17) showed left axis deviation, slurring of the S wave in the third lead, disphasic T wave in the first and second leads and isoelectric T wave in the third lead.

Case XI.—B. Z., male, 53 years old, painter, with an essentially negative past history. He was always a hard worker, a heavy user of tobacco, and of a rather irritable nervous disposition. While at perfect rest one day after his evening meal, he suddenly felt a severe oppression in the epigastrium and precordium, radiating to the neck, together with a cold sweat, vomiting and a sensation of fainting. This subsided in four hours, after the administration of morphine. The following two days he was running a temperature of about 101 F., had marked tenderness over the epigastrium, pulse was very weak and heart sounds poor. His family physician considered his case one of acute cholecystitis. Since that attack, the patient has experienced dyspnea on moderate exertion.

I examined him about five months after the onset, at which time he presented a

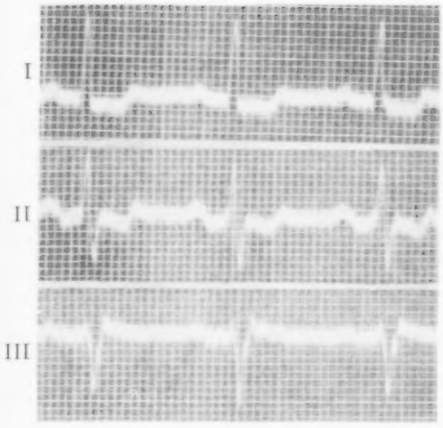

FIG. 17

marked facial pallor. The peripheral vessels were markedly sclerotic. His blood pressure was systolic 150, diastolic 90. The lungs showed a few moist basal râles. The heart was of normal size and shape, rate 65, regular rhythm. The first sound was weak, and was partly replaced by a harsh systolic murmur which was transmitted to the axilla and midsternum.

The electrocardiogram (Fig. 18) showed left axis deviation, slurring and notching of the QRS complex in the second and third leads, and negative T wave in all leads.

Case XII.—M. L., male, 52 years old, tailor, was suddenly seized at work with a severe attack of "heartburn," together with a cold perspiration and a sensation of fainting. It subsided in 20 minutes with apparently no ill effects. Another similar short attack recurred four weeks later. Five weeks after the second attack, while at work, he suddenly felt an excruciating burning in the epigastrium radiating behind the sternum to the neck, as if "hot smoke was rolling up from the stomach to the neck." He fainted and when revived, his whole body was covered with a cold sweat.

Examination revealed an individual in extreme anguish. He was gasping for air, and complained of an extreme discomfort and pressure in the epigastrium radiating to the neck and to the left shoulder. He was very restless, tossed around from side to side, and felt as if he was choking. His color was ashen, pulse almost imperceptible, rate about 110, regular. The heart was markedly enlarged to the right, the first sound was muffled and almost inaudible. The right lung showed almost complete suppression of breath sounds, and numerous moist râles were heard at the bases. The liver extended about four inches below the costal margin. The blood presure was systolic 80, diastolic 70.

An electrocardiogram (Fig. 19) done at that time showed very low voltage curves,

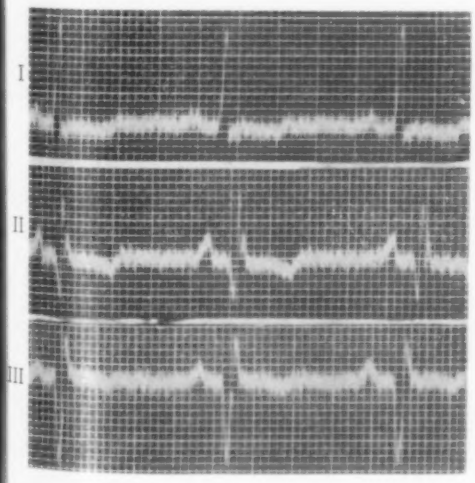

FIG. 18

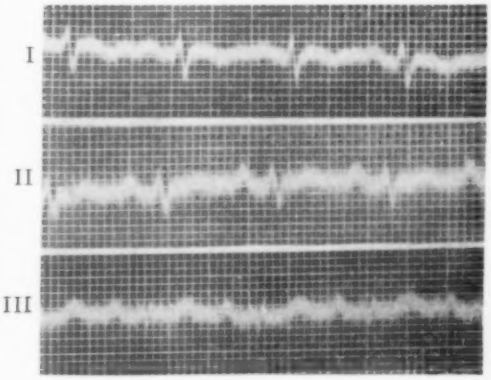

FIG. 19

slurring of the QRS complex in all leads, and rounding of the S-T segment with negative T wave in the first lead.

Three days later there was a definite pericardial friction rub in the lower sternal region over an area 2½ inches wide between the levels of the third and fifth ribs. He showed progressive improvement within the next two weeks. At the present writing, about three months after the last attack, he feels quite well. The heart sounds are of good quality with the exception of a slight muffling of the first sound. The blood pressure is systolic 132, diastolic 88. The liver is normal and the lungs are negative.

The electrocardiogram (Fig. 20) shows higher complexes, and the T wave in lead 1 is isoelectric.

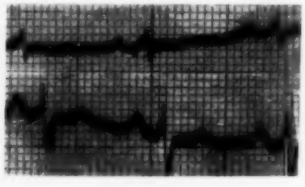

FIG. 20

Case XIII.—M. A. M., male, 52 years old, complained of continuous dull precordial ache and occasional epigastric pain on walking. His father died suddenly at 47 and mother at 50 of causes unknown to the patient. He was always a heavy tobacco smoker.

The present complaint dates back nine months, when taking a cold shower, he suddenly experienced a very sharp pain in the precordium, which subsided on the application of heat. Five days later, he again felt a most excruciating pain in the precordium lasting six hours. The pain came while at rest and was accompanied by great shock. He was confined to bed six weeks.

Examination nine months after that attack showed the heart to be greatly enlarged to the left and also slightly to the right. The first sound was slightly muffled. The lungs showed an occasional moist râle at the bases. The peripheral vessels were slightly thickened and the blood presure was systolic 140, and diastolic 90.

The electrocardiogram (Fig. 21) showed left axis deviation, slight depression of the R-T segment in the third lead, with a definitely negative T wave in the second and third leads.

Case XIV.—S. O., male, 53 years old, plasterer, who was always healthy, suddenly developed severe palpitation with marked precordial oppression and weakness, compelling him to stay in bed a week. One year later he suddenly experienced another attack of severe palpitation and a most annoying pain in the left precordium, radiating to the back. He felt like vomiting and a cold perspiration covered his body. The attack lasted two hours and gradually subsided. Since then he had milder recurring attacks and he noticed that he became very short of breath on the slightest exertion.

Four days after the last severe attack he showed an ashen-brownish color, but he appeared to be rather comfortable. The heart was of normal size and shape, first sound short and split, rate about 58, rhythm regular. The peripheral vessels were markedly sclerotic, and the blood pressure was systolic 120, diastolic 80. An occasional moist râle was heard at the bases of the lungs.

The electrocardiogram (Fig. 22) showed left axis deviation, negative T wave in the first lead, elevation of the S-T segment and abnormally high T waves in the second and third leads.

Seven weeks later the patient felt greatly improved. The heart sounds were of good quality, rate 64, rhythm regular. The electrocardiogram (Fig. 23) still showed left axis deviation, QRS of lower voltage, T wave in the first lead positive, while in the second and third leads, of much lower amplitude.

Case XV.—J. J. Mc., male, 63 years old, heavy tobacco smoker, but whose history is otherwise negative, suddenly experienced a severe precordial tightening while walking. It lasted ten minutes and stopped spontaneously. Towards the middle of the night, he was awakened by a severe, lancinating precordial pain, radiating to both arms, accompanied by cold perspiration and a sensation of impending dissolution. The attack lasted seven hours and was only partially relieved

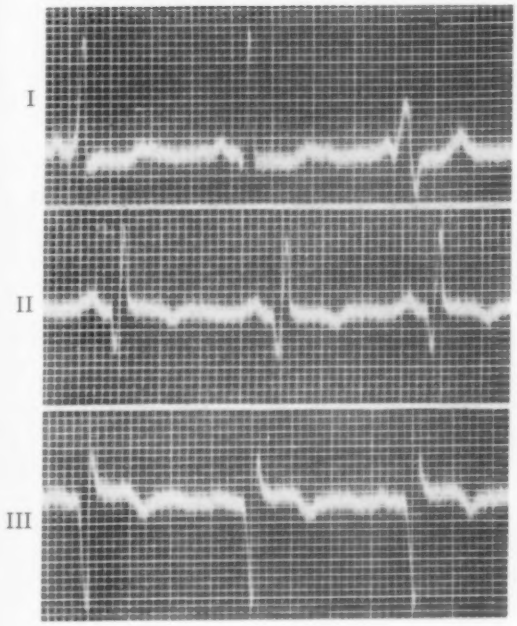

FIG. 21

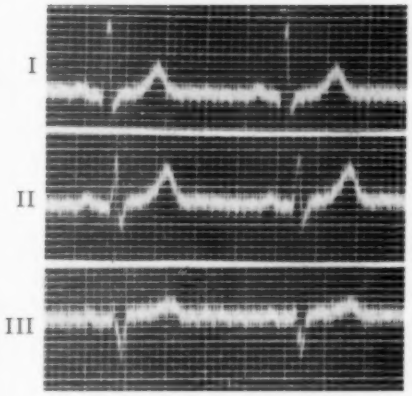

FIG. 23

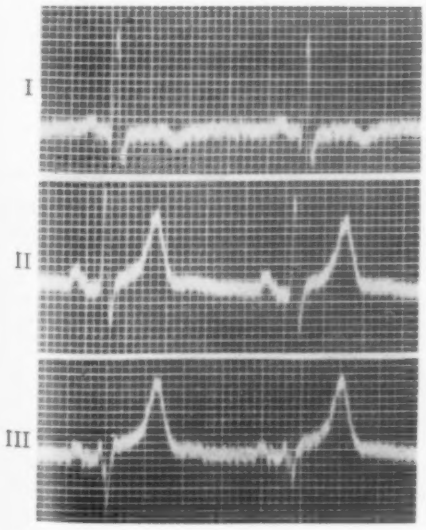

FIG. 22

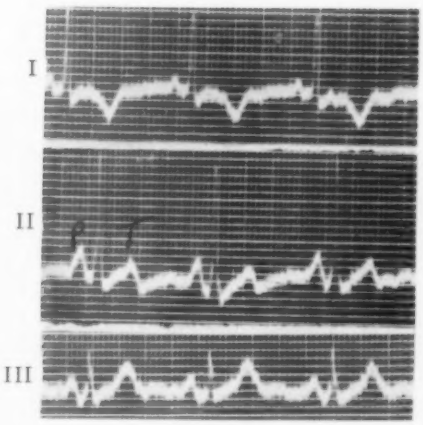

FIG. 24

by morphine. Since then he is experiencing some precordial pain on exertion, radiating to the upper abdomen.

Examination three months after the onset showed a very pale, elderly male with marked peripheral arteriosclerosis. His heart was of the longitudinal type, but no definite enlargement could be made out. The first sound was muffled, rate was 70, rhythm regular. The blood pressure was systolic 160, diastolic 80.

The electrocardiogram (Fig. 24) showed a rounding out and slight depression of the S-T segment and negative T wave in the first lead.

Case XVI.—A. S., male, 60 years old, tailor with a history of precordial pain and oppression on exertion for the past seven years, was suddenly awakened one night with excruciating pain in the upper sternal region radiating to both arms and the back, between the scapulae. The pain lasted three hours, and required considerable morphine for relief. Since then he experienced precordial "tightness" and pain on the slightest effort.

Examination four weeks after the attack showed the heart to be slightly enlarged to the left, rate 88, rhythm regular. There was accentuation and slight splitting of the first sound. The peripheral vessels were markedly sclerotic and the blood pressure was systolic 120, diastolic 90. He was dyspneic and his color was ashen.

The electrocardiogram (Fig. 25) showed left axis deviation, depression of the S-T and R-T segment in the first and second leads, and diphasic T wave in those leads.

Case XVII.—M. S., male, 74 years old, merchant, was suddenly seized two hours after an evening meal, with severe epigastric pain, radiating to the retrosternal region, associated with marked belching and cold sweat. The attack lasted eight hours. The following three days he was running a temperature of 100 to 101½ F., heart was regular, sounds of poor quality, rate 100.

I saw him two weeks after the attack when he revealed nothing abnormal except for muffling of the first heart sound, and a few moist râles at the bases of both lungs. The electrocardiogram (Fig. 26) showed left axis deviation, slight rounding of the S-T segment, negative T wave in the first lead, and splintering of the QRS complex in the third lead.

Case XVIII.—J. V. L., male, 60 years old, clerk, complained of palpitation, epigastric heaviness, pain in the apical region of the heart and weakness, following any exertion or coming on after a meal. He was always a heavy cigarette smoker, and was told four years ago that he had hypertension.

The present complaints followed an attack of "acute indigestion" two years ago, characterized by sudden epigastric pain with heaviness, belching, and extreme palpitation, as if someone was "bouncing" him over his heart. His entire body was "drenched." The condition lasted eight hours.

Examination, two years after that incident, showed an obese individual, slight exopthalmos, teeth infected, tonsils enlarged and diseased. The bases of the lungs showed an occasional moist râle. The heart was greatly enlarged to the left, and the aortic arch was markedly widened. The first sound was

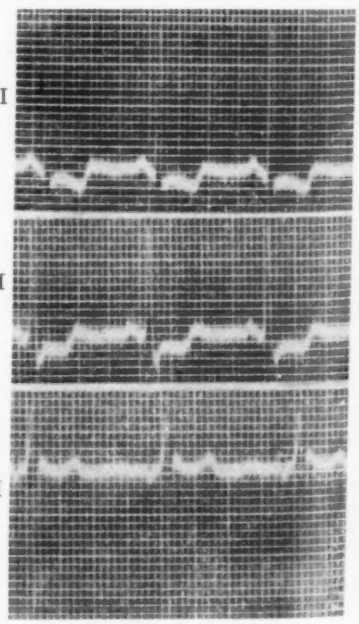

FIG. 25

long, muffled and split and a rough systolic murmur was heard over the aortic area, transmitted to the apex. The peripheral vessels were markedly sclerotic, and the blood pressure was systolic 160, diastolic 100.

The electrocardiogram (Fig. 27) showed left axis deviation, slurring of the QRS complex in all leads, rounding of the S-T segment and negative T wave in the first and second leads.

Case XIX.—A. W., male, 62 years old, waiter, gave a history of chancre 22 years ago for which he was treated with salvarsan. For the past few years he was subject to a productive cough, slight headache, occasional dizziness and slight shortness of breath on exertion.

On the day of examination he suddenly experienced a burning sensation in his throat and epigastrium with a sharp pain in the left shoulder. He became markedly prostrated and collapsed.

Examination revealed an elderly male in marked agony. His skin and mucous membrane were pale, pupils were contracted and

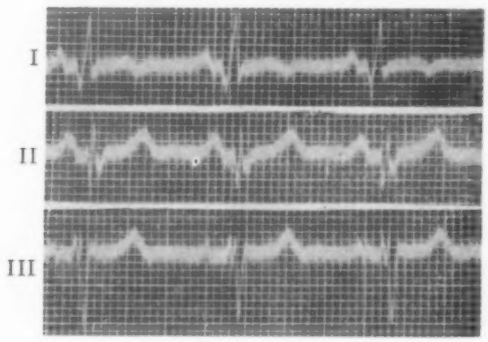

Fig. 26

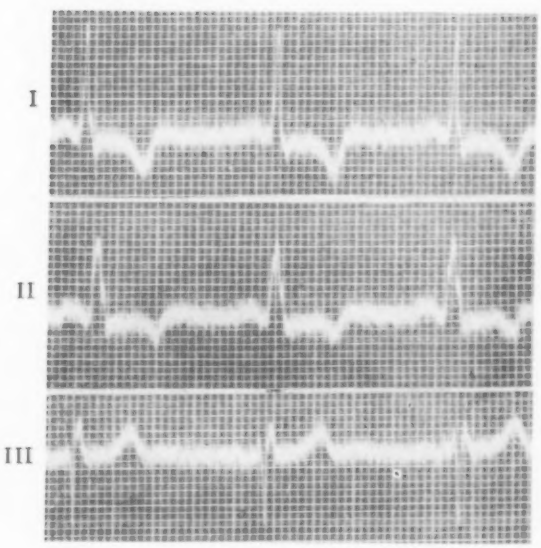

Fig. 27

reacted sluggishly to light. The peripheral vessels were markedly sclerotic, the finger tips cyanotic and clubbed. Respirations were labored. The heart was of normal size, regular rhythm rate about 40, sounds almost inaudible. The lungs showed emphysematous breathing and numerous râles were heard. The abdominal wall was markedly rigid, especially the right rectus muscle. The white cell count on the second day was 11,800, with a differential of 80% polymorphonuclear leucocytes. The blood chemistry showed urea nitrogen 30, creatinin 2.5, uric acid 6.5 and glucose 120 milligrams per 100 c.c. The blood Wasserman was negative. The urine showed considerable albumin, many hyaline and coarsely granular casts.

The electrocardiogram, done on the second day (Fig. 28), showed marked sinus bradycardia, low voltage QRS wave, left axis deviation, isoelectric T wave with tendency towards being negative, in the first lead, and high R-T takeoff in the second and third leads.

He subsequently showed progressive improvement. His temperature ranged between 97 and 99 and the pulse rose to 70 and became more full.

I saw him again on May 2nd, 1930, at which time he felt well, and was working for three weeks as waiter, without any discomfort. The heart sounds were of fair quality. The electrocardiogram at that time (Fig. 29), still showed low voltage curves, but there was no left axis deviation. The T wave in the first lead was definitely negative, and the R-T interval in the second and third leads returned to the iso-electric line. There were occasional premature contractions originating in the right ventricle.

Case XX.—I. M., male, 60 years old, tailor, hypertensive of several years standing, and subject to occasional precordial pain for the past five years, appearing on exertion. A year ago he had a sudden attack of severe precordial pain, radiating to the back, associated with cold sweat and collapse. The pain lasted one hour and gradually subsided. This was followed six months later by another similar attack, and a third attack three days ago. The last attack was associated with extreme dyspnea, belching, cold perspiration and collapse.

Examination at this time revealed a markedly dyspneic male, with anxious look, tossing around from side to side due to marked discomfort. His color was ashen. The heart was enlarged to the left, rate 44, regular. The first sound was very weak and was replaced almost entirely by a systolic murmur heard best at the apex and transmitted to the axilla. The peripheral vessels were moderately sclerotic, pulse weak, and blood pressure systolic 120, diastolic 80. Previously, his blood pressure was over 200 systolic. The electrocardiogram (Fig. 30) showed 2:1 heart block. The auricular rate was 88, ventricular rate 44. There was left axis deviation. The S-T segment was depressed in the first lead and the R-T segment elevated in the third lead. The T wave seemed to be of the plateau-shaped type in the third lead, and negative.

Discussion

The clinical and electrocardiographic phenomena of acute coronary occlusion are dependent upon two underlying manifestations: (a) suddenness of onset, and (b) nature of damage.

Clinical Manifestations

Suddenness of Onset—What the determining factors are in the sudden onset of thrombotic or endarteritic occlusion of a vessel is still a debatable question. We can readily understand how sudden embolic occlusion might occur, but such being comparatively rare, we must still speculate on the causes of the sudden onset of the greater number of cases of occlusion. That it is the abruptness of onset, however, which is responsible for the greater part of the clinical picture is evidenced by the fact that chronic coronary occlusion with a gradual obliteration of as much as three-fourths of the

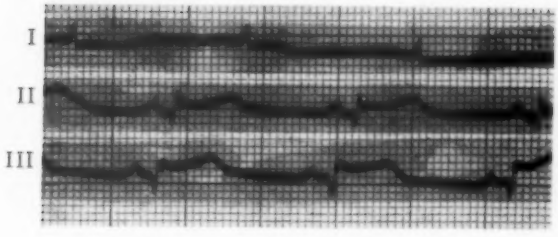

FIG. 28

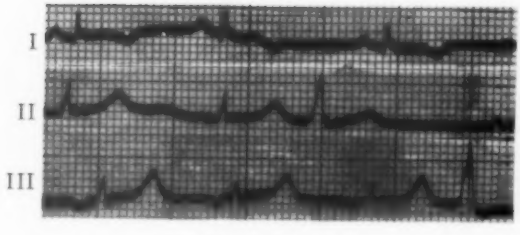

FIG. 29

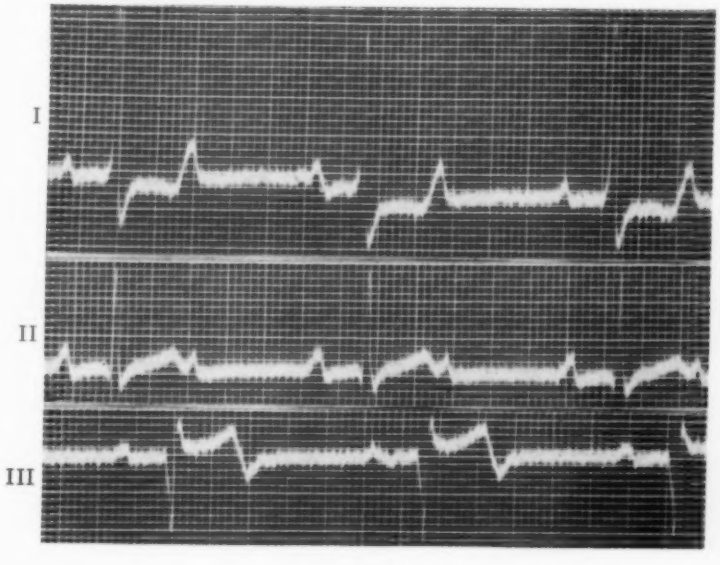

FIG. 30

coronary system may occur with comparatively little discomfort, as shown by Osler[1]. It is of interest also to note that in many cases with typical symptoms of acute coronary occlusion reported by various authors, the post mortem examination did not reveal complete occlusion. A marked narrowing of a vessel by an atheromatous plaque with infarction of the portion of the heart supplied by that vessel were the usual findings in such cases. What determines the acuteness of symptoms is hard to tell. I would suggest the possibility of a sudden onset of edema in the vessel wall or in the intima overlying the atheromatous area, completely occluding the vessel during life and subsiding by the time the heart is examined, post mortem.

The acuteness of onset gives rise to a train of reflex phenomena which may be grouped under (1) so-called status anginosus or status asthmaticus of the European writers, and (2) shock.

Status anginosus is characterized by excruciating pain of variable duration of hours or days, usually situated in the retrosternal region, but it may be located mainly in the epigastrium, which some authors term "status gastralgicus," or it may be felt over the whole precordium. From its seat of greatest intensity, the pain may radiate to the left shoulder, left arm, both arms, back of chest, neck, left leg, or to two or more of those areas. In the twenty cases here reported, five had their greatest intensity of pain at the sternal region, five in the precordium, three in the epigastrium, two in the epigastrium and retrosternum, one in "both breasts." The radiation occurred in three cases to the left shoulder, in one case to the left arm, leg and back, in one to the throat, in four to both arms, in one to the back between the scapulae, in one to the neck, in one to the neck and left shoulder, and in seven there was no transmission. In some of these there was no actual pain.

Instead of pain, there may be severe precordial or retrosternal tightness, marked epigastric oppression and gaseous eructation, or severe burning sensation in the precordial or epigastric region with nausea and vomiting. One of our patients complained of excruciating "heartburn" as if "hot smoke was rolling up from the stomach to the neck." Another complained of severe burning sensation in the epigastrium and throat, associated with pain in the shoulder. One experienced very severe epigastric oppression, and another, severe "tightness."

Shock is a second manifestation due to suddenness of onset. The marked reflex vasomotor disturbance produces a fall in blood pressure to an abnormally low level. This results in dyspnea, or even Cheyne-Stokes breathing, fainting, marked prostration, characteristic pallor or ashen color, marked sweating and coldness, weak pulse, feeble cardiac impulse and sounds, and the suppression of urine. That it is a reflex vasomotor disturbance, not the damaged heart, which is responsible for these manifestations — even the feeble cardiac impulse and weak sounds — is evidenced by the fact that many of these symptoms abate or diminish in intensity a day or two after the onset, at a time when the myocardial destruction is greatest. It is very likely also that it is the impoverishment in

the coronary blood supply due to the fall in blood pressure, which is responsible for the myocardial failure and the resulting signs of passive congestion, always present to a greater or less degree.

Nature of Damage—This is responsible for the greater part of the objective phenomena which complete the clinical picture, as well as for the electrocardiographic manifestations.

Infarction of the myocardium, resulting from coronary occlusion, gives rise to reactive processes — inflammatory, exudative and absortive in nature — producing more or less fever and leucocytosis in the early stages. If the infarction extends to the pericardium, a reactive exudative pericarditis will result, producing the characteristic pericardial friction rub which is occasionally heard. The infarction more often reaches the endocardium, producing reactive endocarditis to which mural thrombi become attached. These may serve as emboli, and embolic phenomena are therefore frequent in this disease. Pulmonary embolism, resulting in pulmonary infarction, is most common. It occurred in two of our cases. The irritative and reactive processes of the myocardium also result in disturbances of rate and rhythm. The majority of cases show sinus tachycardia. In some cases, such as 19 and 20 of our series, there is a marked bradycardia. This gradually mounts to normal with improvement, as in case 19. The bradycardia may be of sinus origin or due to block. In the latter case, the auricular rate may be rapid. Occasionally the disturbance in conduction is transient, in which case it is most likely due to edematous infiltration around the conducting system, which subsides. Gallop rhythm is a very frequent finding. Of the arrhythmias, the most common are premature contractions, but flutter, fibrillation and paroxysmal tachycardia were observed.

Electrocardiographic Evidence

In a person past 30 years of age, with sudden onset of the characteristic anginal syndrome, fainting, marked fall in blood pressure, characteristic color, muffled heart sounds, with perhaps, gallop rhythm and various forms of arrhythmia, followed later by some rise in temperature, leucocytosis, and possible pericardial friction rub, the diagnosis of coronary occlusion may be made with certainty. We have, however, the additional help of the electrocardiogram.

In 1909, Eppinger and Rothberger[2], described the alterations in the QRS and T waves caused by destroying part of the left ventricular musculature by silver nitrate. A current of injury was set up resulting in a monophasic curve. No definite T wave was evident, but the R-T segment rose high on the descending limb of the R wave and came down in a curved fashion to the isoelectric line. As repair of the damaged muscle took place, the R-T deviation gradually came down to the isoelectric line, and a definite T wave was formed.

In 1918, Smith[3] produced experimental occlusion of the coronary arteries by ligation. The electrocardiogram showed fairly constant T wave changes, from markedly positive soon after ligation to markedly negative in about 24 hours. This was followed by an iso-

electric T wave which again became positive on about the seventh day. The size of the positive and negative phases as well as the height of the R-T interval were in direct proportion to the size of the artery ligated. At the end of four weeks, the T wave again became isoelectric or negative in one or more leads.

In 1920 Pardee[4] described similar T wave changes in a clinical case. Early there was a high R-T level, followed by its gradual lowering and rounding, and final production of a negative T wave. The R-T deviation has since been labeled "Pardee's Coronary Occlusion T wave."

In the same year, Smith[5] showed that the greatest negativity in the T wave occurred in those dogs where the blood supply to the apex was affected greatest. He reported three years later[6] the electrocardiographic findings of 11 patients with coronary occlusion where the T wave changes were similar to those of experimental occlusion.

Wearn[7], on the other hand, in a series of 19 autopsy cases of coronary thrombosis and myocardial infarction, found only one record with typical R-T changes. The other electrocardiographic findings were those of premature contractions, block, auricular fibrillation, delayed QRS conduction, and in two cases, perfectly normal curves. His conclusions were that "no one form of electrocardiogram is characteristic of this condition." He adds, however, that no definite conclusion can be drawn from his series, as there was a variation in time of relationship between the onset and record taking, in the different cases.

Parkinson and Bedford[8], analyzing the electrocardiographic tracings of 100 cases of coronary thrombosis, found deviations in the R-T and S-T segments occurring early in most cases, and a negative T wave followed later. The R-T and S-T elevations and depressions were best seen in the first and third leads, and were opposite in direction. The T wave in some cases became evident before the R-T segment returned to the iso-electric line, in which case the direction of the T wave was always opposite to that of the R-T segment. The authors believed that if the R-T deviation lasted several weeks, it pointed towards the extension of the infarct — the usual duration being one week. They divided the T wave changes into "Type One," where it is negative in the first lead, or in the first and second leads, and "Type Three," where it is negative in the third lead or in the third and second leads. They further added that there may be atypical T wave changes such as inversion in all leads, or a normal T wave, which may be due either to recovery or to infarction occurring in a "silent area" as far as the T wave changes were concerned.

Barnes and Whitten[9], in twenty-one cases with "Type One" T wave, found the infarction to occur in the anterior and apical portion of the left ventricle, in the region supplied by the left coronary artery. In six cases with "Type Three" T wave, infarction occurred in the posterior portion of the left ventricle, in the region ordinarily supplied by the right coronary artery. In four cases of the mixed type, infarcts were found in both, the anterior

and the posterior portions. Shifting type indicates new infarction.

In the cases presented in our paper, seven showed definite R-T elevation or rounding in the third and second leads, with corresponding depression in the first lead. In all these cases, the T wave was fully developed, and was of "Type Three." In two of these, the R-T segment was still above the isoelectric line four weeks after the onset, and no clinical evidence of extension of infarction was present. In another case (Case 13), such deviation was present nine months after the onset. The electrocardiograms of four other cases approached the "Type One" T wave, although not typically so in all cases. One of these (Case 18), showed some depression or rounding of the S-T segment in the first and second leads two years after the onset, but there is reason to believe that he had fresh myocardial infarction at the time the tracing was done. Case 19 showed a high R-T segment in the third and second leads but the developed T wave was not opposite in direction to the R-T segment.

The remaining nine cases of our series did not show any typical R-T or S-T deviation, and no constant T changes. Case Four, for instance, had the R-T and S-T segments above the isoelectric line in all leads. Case Six, showed practically no elevation or depression of the R-T segment three days after the onset. Ten weeks later, however, during which time he felt quite comfortable, and the physical findings were negative, he showed some depression and rounding of the S-T segment in the second and third leads, a lower T wave in the first lead and a negative T wave in the second lead.

Case Fourteen showed a high S-T segment in the third and second leads, with a markedly accentuated T wave in those leads, and a negative T wave in the first lead, four days after the onset. Seven weeks later, there were positive T waves in all leads and, except for the axis deviation and some slurring of QRS, the tracing appears perfectly normal. I feel, however, that this is merely an intermediary stage, and that he will develop a "Type Three" tracing.

The other findings of note are: (a) Very low voltage QRS complexes in Cases Twelve and Nineteen, with increase in such voltage in Case Twelve, on improvement. (b) Extremely deep T wave in Case Five, becoming less so as the patient improved. (c) Auricular fibrillation, Case Three. (d) Diminished height of the R wave in the third lead and depth of the S wave in the first lead in Case Two, two weeks after the first tracing. (e) Change in the electrical axis from left to right, in Case Nine. (f) First and second degrees heart block, in Cases One and Twenty respectively.

The conclusions we may draw from our electrocardiographic findings, as well as from those of the references mentioned, are that although the so-called "Coronary Occlusion T Wave" may be considered to be pathognomonic when present *in association with a typical or somewhat atypical clinical picture* of coronary occlusion, its absence does not rule out such occlusion, for it is more frequently absent or anomalous than present. Furthermore, its presence is not always indicative of

coronary occlusion, as it has been found in such conditions as rheumatic myocarditis, by Cohen and Swift[10]; in rheumatic pericarditis, by Porte and Pardee[11]; and, in massive pericardial effusion, clinical and experimental, by Scott, Feil and Katz[12]. It is at best a finding of peculiarly localized myocardial damage, due to occlusion if the clinical picture points towards that condition, at which time it is conclusive evidence.

I would consider the most important electrocardiographic evidence of coronary occlusion the *frequent alterations* in the make-up of the electrocardiogram, in periods of days or weeks. Of these the most significant are the changes in position and configuration of the R-T and S-T segments and the T wave. Of the latter, its exaggerated height, followed by gradual depression and final negativity, are significant. Significant also are the alternate negativity and positivity of the T wave in various leads from time to time, during comparatively short intervals, during some phases of which the electrocardiogram may even appear to be perfectly normal, and rather misleading in the diagnosis. Repetition of the tracing, however, at a later time will give us the true state.

Other significant changes from time to time are: (a) High voltage QRS waves followed by markedly low voltage, which again increases later; (b) Change in the direction of the electrical axis from left to right, and vice versa; (c) Appearance and disappearance of block; (d) Appearance and disappearance of premature contractions; (e) Variations in the heights of the various components of the QRS complex from time to time.

These findings and changes are well demonstrated in our cases, as well as in two cases reported by Willius[13], and in the experimental and clinical cases reported by the authors quoted elsewhere. If no other electrocardiographic evidence is found, the frequent alterations of whatever complexes are present may be considered to be pathognomonic. Acute myocarditis, of rheumatic or other infectious origin, may also produce frequent changes in the electrocardiogram corresponding with the spread of the inflammation, its localization, and its subsidence. The clinical picture, however, as well as the age of the individual—occurring usually in earlier life—will help us in the differential diagnosis.

Summary

Twenty cases of acute coronary occlusion are reported, and the clinical manifestations as well as the electrocardiographic findings are discussed.

The clinical and electrocardiographic phenomena are dependent on the acuteness of onset, and the character of the damage. The former gives rise to the anginous syndrome and shock, with its concommitant manifestations. The latter is responsible for the objective phenomena, such as fever, leucocytosis, pericardial friction rub, embolic phenomena and electrocardiographic changes.

The outstanding features of the electrocardiogram are the frequent changes in the configuration and level of the R-T and S-T segments, and the configuration of the T wave. Less

frequent, but equally important, are variations in the height, conduction time and configuration of the QRS complex; changes in auriculo-ventricular and interventricular conduction, and in the direction of the electrical axis, at various times in the course of the disease. Emphasis is to be laid on changes in the components of the electrocardiogram, rather than on any single finding no matter how significant it may be.

References

[1]Osler, W.: Angina Pectoris, Lancet, Mar. 26, 1910.

[2]Eppinger, H. and Rothberger, C. J.: Wien. Klin. Wchnschr., 22:1091, 1909.

[3]Smith, F. M.: Ligation of the Coronary Arteries with Electrocardiographic Study, Arch. Int. Med., July, 1918, 22:8.

[4]Pardee, H. E. B.: Electrocardiographic Sign of Coronary Artery Obstruction, Arch. Int. Med., 26:244, Aug., 1920.

[5]Smith, F. M.: Further Observation of the T Wave Following Ligation, Arch. Int. Med., 25:673, June, 1920.

[6]Smith, F. M.: Electrocardiographic Changes Following Occlusion of the Left Coronary Artery, Arch. Int. Med., 32: 497, Oct., 1923.

[7]Wearn, J. T.: Thrombosis of the Coronary Arteries with Infarction of the Heart, Amer. J. Med. Sc., 165:250, Feb., 1923.

[8]Parkinson, J. and Bedford, D. E.: Successive Changes in the Electrocardiogram after Cardiac Infarction (Coronary Thrombosis), Heart, 14:195, Aug., 1928.

[9]Barnes, A. R. and Whitten, M. B.: Study of the R-T Interval in Myocardial Infarction, Amer. Heart Jour., 5:142, Dec., 1929.

[10]Cohen, A. E. and Swift, H. F.: Electrocardiographic Evidence of Myocardial Involvement in Rheumatic Fever, J. Exp. Med., 39:1, 1924.

[11]Porte, D. and Pardee, H. E. B.: The Occurence of the Coronary T Wave in Rheumatic Pericarditis, Amer. Heart J., June, 1929.

[12]Scott, B. W., Feil, H. S. and Katz, L. N.: The Electrocardiogram in Pericardial Effusion, Amer. Heart J., 5:68, Oct. 1929.

[13]Willius, F. A.: Infarction of the Myocardium, Report of Two Cases, Atlantic Medical Jour., 29:3, Oct., 1925.

A New Esophageal and Cardiospasm Dilator

By Moses Einhorn, M.D., *New York*

CARDIOSPASM has been defined as a spasm of the musculature of the cardia or epicardia sufficient to cause either partial or complete obstruction to the passage of food from the esophagus into the stomach. The subject of the treatment of this condition has occupied the attention of clinicians throughout the world, and the only effectual results were obtained by a series of intermittent dilatations by means of rubber balloon dilators operated by hydrostatic or pneumatic pressure. Some, particularly Starck[1] and Schreiber[2], have preferred using mechanical divulsors, inserted through the esophagoscope, under the guidance of the eye and the sense of touch.

Bougienage was for some time employed, small bougies first being introduced, and gradually increased to the largest size. The bougies were left in position and in contact with the stricture, and drawn frequently through the cardia, at each treatment. Leyden successfully employed permanent cannulas, which remained in situ for several days. These cannulas were introduced with the aid of the stomach tube. They were from six to eight centimeters in length, and were attached by means of strong cords to the ear or around the neck.

In latter years, dilatation by air and water has been advocated, as suggested by Plummer[3], Sippy[4], Mosher[5], and Vincent[6]. These dilators are similar in construction, consisting of a long rubber tube, 34 French in diameter, with a conical metallic acorn at the lower end. Several holes are perforated within a few inches of the bottom of the tube, and this section of tubing is encased in a rubber bag, covered with another silk or linen bag, and an additional layer of thin rubber. A silk thread is used in some of these dilators, as a special means of guiding the metallic acorn through the cardiac orifice. Zohlen[7] introduced a flexible dilator with a series of expansible olives, but judging from the description, the apparatus appears rather complicated in structure.

Surgery as a means of treatment was employed with successful results, by numerous surgeons including Mikulicz[8] and Erdmann[9]. Gastrostomy was usually performed, followed either by digital dilatation of the spasmodic area from below upwards, or by introducing long curved forceps, the blades, covered with rubber.

In a recent article[10], I advanced gastric feeding as a new treatment for cardiospasm, and had great success with same in the treatment of patients suffering with a mild degree of esophageal spasms. In this treatment, I use my new gastroduodenal apparatus[11], which consists of a special bucket

and a marked tube. The main characteristics of the bucket are its three part composition; its capsular shape, spiral arrangement and its lower part three times heavier than the upper part. The patient is fed with the aid of the tube for a period of ten days, and during this period, remains in bed with the inserted tube, in order to insure complete rest and relaxation. The treatment, may however, be ambulatory. Every three days, preferably in the morning, on an empty stomach, the tube is removed for cleansing purposes. It is first removed but a few inches, and the saliva which has accumulated in the esophagus above the spasmotic area is withdrawn with a syringe. The esophagus is then thoroughly washed, by injecting a solution of boric acid or luke warm water through the tube. After repeating this process several times, the tube is removed, cleansed with warm water, and re-inserted into the stomach.

The feedings should be frequent and in small quantities, not exceeding one and a half (1½) glasses every two or three hours. Sharp and spicy foods should be avoided; also, extremes in heat or cold. Water may be taken through the tube between meals, and thirst and dryness of the mouth satisfied with the aid of a mouthwash. The diet consists of orange juice, grape juice, tea, cocoa, chocolate, coffee, milk, cream mixture, (¾ milk, ¼ cream), tea and milk, egg-nog, farina, vegetable soup, celery soup, asparagus soup, chicken soup, barley soup, gruel, beef juice, spinach (liquid form), jello, custard, apple sauce and fruit sauce.

The above treatment offers the following advantages:

1. Complete rest is offered to the spasmodic area, including the lower part of the esophagus.

2. The patient is free from discomfort, in the epigastric region, usually accompanying cardiospasm.

3. The intake of food can be increased with the aid of the tube, and weight incidentally gained.

4. Physical and psychic rest obtained by this treatment indirectly has a beneficial effect on the cardiospasm.

5. The constant presence of the tube at the site of the spasmodic area, tends to counteract the spasms.

In certain cases, however, gastric feeding is insufficient in the treatment of cardiospasm, and intermittent dilatation by special instruments is often necessary. I had occasion both here and abroad, to use the numerous devices heretofore mentioned, but in each case I found the same mechanically unsatisfactory. Besides being bulky and uncomfortable for the patient to retain, the danger of perforation of the esophagus was encountered in the use of these appliances.

I observed particularly, in my study of cardiospasm, that the spasms were usually unequally distributed, and that the highest degree of spasticity was generally present at the cardiac opening. I was also impressed by the excellent results obtained by surgeons in manual dilatation of the cardia from below upwards and laterally, and therefore concluded, that in order to dilate the spasmodic area mechanically, the strength of dilatation should be applied from below upwards and laterally, and not from above downwards. As a result of this observation and study, I

devised an apparatus on the basic principles of lateral and retro-dilatation.

My cardio-dilator apparatus (Fig. 1-A), consists of a special bucket, a tube, a rubber bag, and a syringe. The bucket (Fig. 2), is one inch in length, 11 grams in width, and 27 French in diameter. It is of capsule shape, with an obtuse point and is composed of three divisions: (a) neck (b) shaft (c) bottom.

A. *The Bucket.*

(a) The neck, through which a large opening is bored, serves as an outlet to the hollow chamber at the bottom of the bucket, to which the tube and small rubber bag are attached.

(b) The shaft has a groove ⅛ inch in width, to which the rubber bag is fastened. A canal drilled through the shaft, connects the neck with the bottom of the bucket.

(c) The bottom, consists of a hollow chamber, which contains four openings for the passage of the fluid. This perforated chamber is connected to the neck by a large canal drilled through the shaft. A wire, soldered at one end to the bottom of the bucket, passes through the canal and the neck, and extends the entire length of the tube. The wire is soldered to a small metal connection at the outer end of the tube.

B. *The Tube.*

The tube (Fig. 1-A) is 12 French in diameter, semi-soft in quality and is 28 inches in length. It is marked off by a heavy black line 24 inches from the bucket. At the outer end of the tube is a small metal connection, to

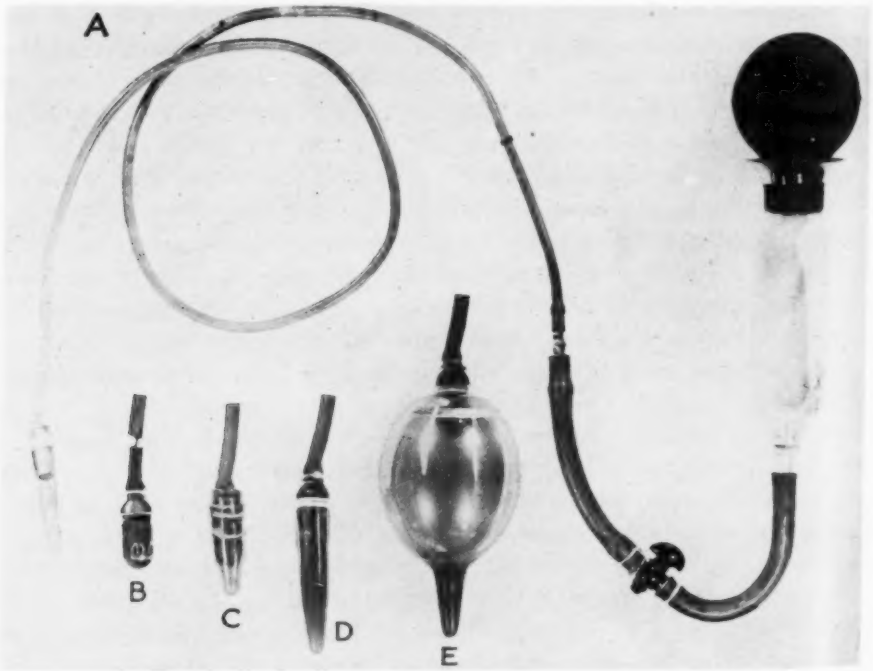

Fig. 1

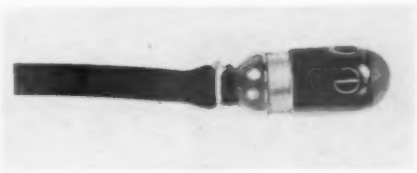

FIG. 2

which the wire which passes through the tube is soldered. Two additional pieces of rubber, separated by the insertion of a rubber stop-cock are connected to the tube at this point. The rubber stop-cock is introduced to regulate the flow of the fluid through the tube and into the bag. The wire which extends through the tube, reinforces it, and tends to supply the resistance necessary when force is employed to overcome the spasmodic area, and also to withdraw the bag in the process of retro-dilatation.

C. *The Rubber Bag.*

The small rubber bag is 2½ inches in length, conical in shape and fits over the bucket, where it is securely fastened with a silk thread at the neck and the groove. It possesses special elastic qualities suited for the purpose, and can be dilated to the extent of 2½ or more inches in diameter.

D. *The Syringe.*

The syringe, used with the apparatus, should be of large size, and preferably graduated.

Method Employed:

Prior to introducing the apparatus, the small rubber bag is inflated with air and gently folded back over the bucket (Fig. 1-C). The patient, who has been instructed to report on an empty stomach, is placed in an upright position on a chair, and is ordered to open his mouth. The bucket, which has been previously moistened, is held between the operator's thumb and forefinger, the middle finger being used as a base, and is placed on the tongue of the patient. After the bucket has been balanced, the patient is instructed to utter the sound AH. The tube is pushed quickly, and the patient concentrates on the act of swallowing. Due to its weight and capsular shape, the bucket will slowly be carried down through the esophagus to the spasmodic area. The tube is then swallowed to within three inches of the mark, and if resistance is encountered, the operator, holding the tube and wire taut, forcibly presses same forward, overcoming the spasmodic area. The tube is now swallowed until the mark is reached, and the patient is fluoroscoped, the various steps in the process of dilatation being carefully followed.

When the tube is observed to have entered the stomach (Fig. 3), a little air is injected through the syringe, causing the folds of the rubber bag to slip down from the bucket (Fig. 4 and Fig. 1-D). The syringe is removed and filled with a mixture of barium, about 4 cc. of which is injected into the tube, inflating the bag to about the size and shape of an egg (Fig. 5 and Fig. 1-E). The stop-cock is immediately closed to prevent the return of the barium to the syringe, and the tube is withdrawn until the cardiac sphincter is encountered and resistance is felt by the patient. A piece of adhesive tape, indicating the distance from the mouth to the cardiac opening of the stomach, is attached to the tube at the point of contact with the mouth.

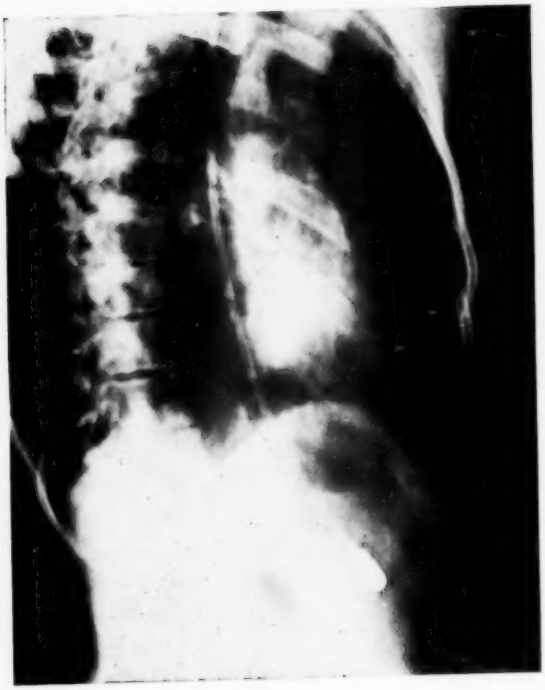

FIG. 3

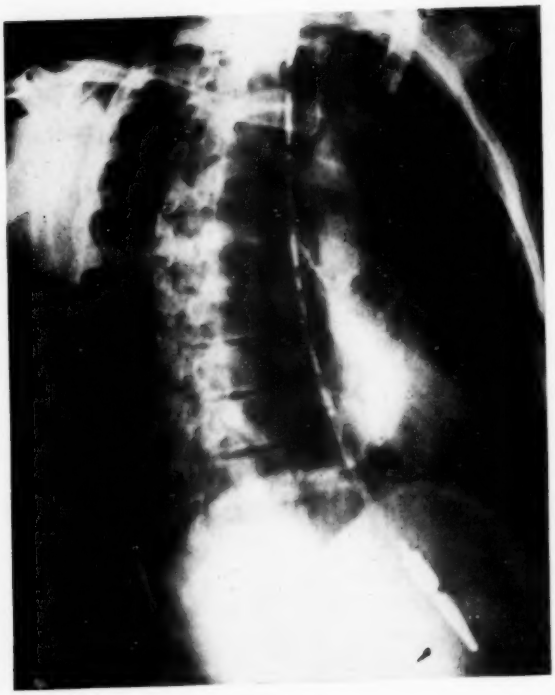

FIG. 4

The stop-cock is now released and a little of the fluid is returned to the syringe. The dilating bag is thus decreased in size, and retro-dilatation is commenced, gentle and continuous traction being applied to the tube and the wire. Slowly the sphincter begins to yield to the wedge-like action of the rubber bag, permitting the upper part to pass through the spasmodic area. By pushing the tube the rubber bag is slipped back into the stomach. The stop-cock is then released, a little more of the barium is injected, and the process of retro-dilatation is repeated.

In order to dilate the spasmodic area laterally, the barium is again siphoned into the syringe. The tube is then withdrawn about an inch, bringing the rubber bag directly in the spasmodic area. About 2 cc. or more of the barium is injected, and the rubber bag is inflated, producing lateral dilatation. The procedure is usually accompanied by pain; if pain is not felt by the patient, the rubber bag has either been insufficiently dilated, or has probably slipped back into the stomach. The bag is allowed to rest at the spasmodic area for a period of five minutes. When the dilatation becomes too painful, part of the barium is withdrawn in order to reduce the size of the inflated bag. This process is continued for a period of 20 minutes, at five-minute intervals, and should be repeated every three days.

Fluoroscopy is necessary only during the first dilation, to determine the length of tubing to be swallowed in order that the dilating bag extends be-

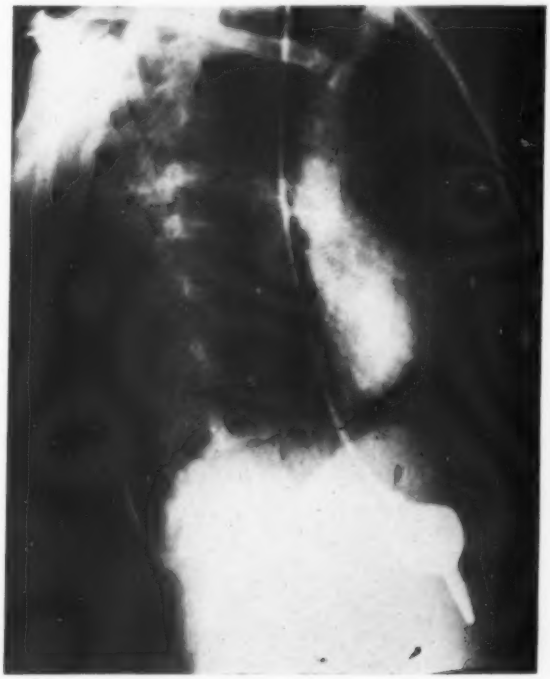

Fig. 5

yond the spasmodic area. Thereafter, the exact location is ascertained by the markings on the tube, the degree of dilatation being measured by the cubic centimeters of fluid injected into the dilating bag.

Advantages:

1. It is simple in construction, inexpensive and not bulky.

2. It is easily swallowed without trauma to the esophagus.

3. No danger of perforating the esophagus.

4. It can be comfortably retained by the patient for some length of time.

5. The use of a silk thread guide is eliminated, as the bucket acts as a guide.

6. Air and water pressure gauges are eliminated.

7. Lateral and retro-dilatation can be accomplished.

8. The degree of dilatation of the rubber bag is ascertained by the volume of fluid injected from the syringe into the dilating bag.

9. It is simple in technique, and can be readily operated both by the physician and the patient.

REFERENCES

[1]Starcke, H.: Miinchen, med. Wchnschr., 1924, 11:334.

[2]Schreiber: Archives fur Verdkr., 192, 8.

[3]Plummer, H. S.: Cardiospasm, with a report of forty cases. J. Am. M. Assn., 1908, li, 549:554.

[4]Sippy, B. W.: The Geo. Blumer edition of Billings-Forchheimer's Therapeusis of Internal Diseases, Vol. IV, p. 473.

[5]Mosher, Harris P.: Cardiospasm, Penn. M. J., xxvi, 240, January, 1923.

[6]Vincent, P. P.: A case of cardiospasm with dilatation and angulation of the esophagus. Med. Clin. N. Amer., 1919-1920, iii, 623:627.

[7]Zohlen, J. P.: A new collapsible esophageal and cardiospasm dilator, Wis. Med. Jour., XXVII, 4, 168:171, April, 1929.

[8]Milkulicz, J.: Zur Pathologie und Therapie des Cardiospasmus. Deutsche med. Wchnschr., 1904, xxx, 17:19; 50:54.

[9]Erdmann, J. F.: Cardiospasm with report of an operative case. Ann. Surg., 1906, xliii, 224:230.

[10]Einhorn, Moses: Gastric feeding as a new treatment for cardiospasm, Ann. Internal Med., vol. 3, no. 11, May, 1930, 1143:1146.

[11]Einhorn, Moses: A new tip for gastroduodenal tubes, J. A. M. A., 1926, vol. 86, pp. 1615:1616.

Pertaining to Peptic Ulcer*

By Anthony Bassler, M. D., *New York*

ONE hundred years ago Cruveilhier showed that gastric ulcer was a clinical entity. Before him (in 1793) Matthhew Baillie wrote about it, and patients complaining of it were described in the 16th century. Thus for 300 years something was known about it, this knowledge for 100 years more fully employed, and in the last 25 years most intimately, and yet really nobody knows much of anything about. Someday, somewhere, somebody is going to tells us accurately what peptic ulcers are caused by, and then we are going to know something worth the while about it, and get somewhere with it. When you have 15 causes for a disease or a condition, the rule is that none of them is right, and until the etiology is known, we are going to be divided into those who do not think, those who think they think, those who think wrong, and those who think.

Regarding symptoms we also are in a chaotic state. In one out of every three new patients I see in my office a diagnosis of ulcer had been made, most of them in a definite way and in a few strongly suspected. Of these about one in twelve have an ulcer in my opinion. There is no condition in medicine in which jumping at diagnosis is more of a continuous hurdle race. Some believe that all you need is an X-ray examination to make a positive diagnosis. Others, like myself for instance, claim this not to be of such value (and might even be misleading) unless there is a history which is suggestive, and unless in deducting from the history and the examinations one constantly remembers that quite perfect ulcer syndromes are present in gall-bladder and appendix disease, upper abdomen adhesions, gastric hypersecretions and mucosal sensitiveness, and some other conditions from which differentiation is essential. To me to make a correct diagnosis of ulcer, especially gastric and lower esophageal, is a difficult matter. Duodenal is much more easy. There are many roentgenologists, practitioners, surgeons, and even gastro-enterologists who diagnose or suspect ulcers far more often than they exist. Contacting such, the patient pays his money and takes his chances, because the average patient, with his or her limited knowledge of medicine, to mention the word "ulcer" is something readily understood, not a few have had told them or suspect that it leads to cancer, so its a good kind of a financial proposition of practice, and if such a man is literarily inclined his statistics of cure are very

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fine, very fine indeed. Now, if we are going to get anywhere worth the while on this subject, an ulcer either exists or it does not, and there should be no twilight diagnosis lit with question and shadowed with doubt. In analytical thought and examinations, the constantly varying clinical picture of this disorder in incidence of pain and measures of its relief, tenderness on pressure, absence or presence of vomiting and its character, bleeding, the X-rays, gastric analyses, and what pertains to penetration, perforation, obstruction, etc. must all be interpreted pivotally as to the diagnosis and relatively as to other conditions which can cause like symptoms and findings. Manifestly, unless all examinations are carefully made, fully done, and wisely evaluated, statistics of neither incidence nor treatment are worth much. In this ulcer question the best of us are only half good enough, and none of us should tickle himself with the vanity of a Roman of being his own God in accuracy, and this applies more for the medical man than the surgeon. Unless in the diagnosis one has proof enough to be sure, so far as ulcer in the science of medicine is concerned, in the words of Moran and Mack it would be better if he "hadn't mentioned it."

Then again no two men agree on much of anything in treatment. There have been advanced 28 different ulcer diets, and they in character and kinds run all the way from animal crackers to the inmates of a zoo. One feeds by rectum to do away with foods irritating the stomach, the next uses a duodenal tube to accomplish the same purpose, and then the next advances, what is popular today, feedings every two hours with foodstuffs of high caloric values to give the stomach lots to do. One claims that to give alkalies is a gross mistake, the next uses little doses of them, and just as good men push the alkalies to the very limit. Long presentations are made on these matters which are about of as much value as porcupine quills on a kangaroo's back. Some state that only the bed treatments are of any value, and others are not insistent on it, and some even, like myself, feel that the ambulatory method in a conscientious patient is often the one of choice. Long discussions, realms of paper, nightly meetings are devoted to these points which are like drops on a window-pane, they run together and trickle away. There are some who believe the subject almost totally medical, with others it is almost totally surgical. Largely the advice given to the patient is tinctured according to the inclination and interests of the doctor. If he is a medical man he visualizes it as a matter of treatment, if a surgeon a matter of operation. Unlike Dean Swift "one ignores the other's bill of fare and yet does not pay the bill of the company."

Now with all these inconsistencies you have asked me to present the subject of the medical treatment of ulcer. How can I do this unless simply to tell you what I do with this condition, and I am probably as much right and wrong as anybody.

In the first place I must be absolutely sure that an ulcer is present. This being so, I search for focal infections in the nasal and paranasal sinuses, throat, mouth and teeth. I may demand that these be attended to before I go any further, or that they be attended

to on the way. On the basis of how long the symptoms have been present, the location and size of the ulcer, in the absence of frank surgical cases and complications, I note whether there is a positive Kahn test, consider the existence and status of anemia, the economic environments of the patient, and consider whether the patient would be best off in bed for three or four weeks, be treated up and around, or operated upon at once. If there is a notch present and it is deep or broad, I occasionally advise bed handling, the same being so in the hemorrhage and secondary anemia cases, and those with bad status of nervous system. Since these comprise only the smaller number of the whole, the ambulatory method is usually followed, and if for any reason they cannot go to bed, I am willing to go ahead with the up and around plan.

In the bed plan, I start with a clearing out of the bowels with calomel and Carlsbad salt, never any other saline because that's the only alkaline one there is, and is one I may advise taking occasionally on the way though. For 24 or 36 hours no foods are taken, small doses of alkalies given while the starvation is on. A reasonable bland diet is ordered with foods taken at three or four-hour intervals; for the first ten days this being totally fluid, and finely comminuted foodstuffs after that. Bathroom privileges are allowed, a Priessnitz or sweat bandage is used for pain (never any opiates) or perhaps a lamp for hourly doses. With the feedings I start with the usually overworked Sippy powders, using the bismuth or the magnesia ones according to bowel movements. As a rule I start with more of the bismuth than the magnesia and usually have to wind up with more of the magnesia. Three times a day the pH of the urine is taken, this being more accurate in the fine gradations of reaction than litmus papers. Any nurse can do this on five minutes instruction. In quantity and size, the powders are given during waking time according to the reactions of the urine, the point being to get the urine just short of pH 7 and never allowing it to become more alkaline than this. The powders are increased until this is accomplished. These tests of the urine compared to the original one and the ones on the way along suggest how much alkali to employ. If the urine, and that means the stomach, too, persists in acidity you can follow the Sippy suggestions in doses, but in nine cases out of ten this is not only unnecessary and unwise but bad therapeutics in addition. Ulcers do not heal well under states of alkalosis, the patient's complaints are a nuisance when toxic symptoms are on, the whole treatment is upset, and it's difficult to get patients quiet again for days. Occasionally belladonna or atropine in small doses is employed, and, of course, a positive or questionable Kahn test adds mercury or the arsenicals hypodermically to the routine.

For the first month out of bed only milk, cream, cereals, bread and butter, simple cakes, jello and such are allowed. In a sense you go back to a more simple dietetic plan than that used at the end of the bed treatment. These foods are added to in the second month, and, as I have originally advanced, more or less dieting in kept up for six months, with alkaline pow-

ders, iron injections, as much rest as possible, perhaps olive oil before meals when the acidity is high and the general condition poor, and in all instances small doses of mercury bichloride and arsenic trioxide three times a day. The stomach is X-rayed each month and the films matched. At a satisfactory result the patient is discharged for the time being with a list of especially irritating foods they must not eat, and told to return if the symptoms recur.

If the X-ray findings or the clinical course do not satisfy me, I suggest an operation at any time. This is the routine treatment even when hemorrhage is or has been present, excepting that morphine and complete physical rest are used in frank bleeding (and morphine is better than all the coagulating blood preparations that ever were advanced) with perhaps the cautious use of blood transfusions. Immediate operation is never advised to control hemorrhage, except when perforation is also present. Sometimes careful lavage with ice water and the administration of four c. c. doses of adrenalin solution are employed.

Everybody agrees as to the value of bed treatment, claiming that as the nervous system is quieted, gastric motility and secretion are controlled. I believe there is some value to it at times, but I doubt that the results compared to the ambulatory treatment are anywhere as great as is believed. With all the other disagreements on this subject it seems poor grace on my part to disagree in any way with the one thing that practically everyone believes in, but we have now handled over 400 cases of gastroduodenal ulcer by ambulatory methods and over 300 by bed treatment, and, after two years time, compared the results in both groups. Figuring especially incidence of operation and return of symptoms, the statistics can be made to show four per cent in favor of the bed method. But these bed cases were a straight line of instances in a period when practically all cases were treated that way, and in them were many more of the milder types than are handled by bed methods today. If these are taken out of the statistics and recomparisons made, the difference is between six and half a dozen. Up to a few years ago, I felt that patients who could not afford to go to bed should preferably be operated upon. After I had a hundred or more walking around with ulcers, not a few supporting families at hard working jobs, and I saw the results accomplished, they taught me that I was wrong in the average case of ulcer and that it was best to try it out their way, and if they had to go to bed, to have an operation as the reason why they went there.

When handled in the ambulatory way, restrictive dieting is not practical. The patient is started with the same food plan as the first month out of bed, and followed for six months just the same. They are taught the litmus paper method of testing urine, alkalies are given according to the reactions, and all of the procedures of the bed treatment are employed. As much physical rest as possible is insisted upon, the Pressnitz or sweat bandage or the lamp being used in the evenings and during Sundays and holidays. X-rays and matching of films is done once a month, the use of tobacco is stopped, exposures to taking colds guarded

against, and the general condition of the patient bucked up as much as possible. As I advanced in 1910, one or two therapeutic doses of x-ray is given over the entire stomach each week for about ten times. This is begun after the bed treatment, or after the second month in the ambulatory. This serves to diminish the running status of acidity, hypermotility and spasm, and to produce a softer, smaller, and more resisting type of scar. Unless operated upon in the interval, observation is continued for six months time. Not a few of the largest and most persistent ulcers have done well on this up and around method.

In 1910 when the Mayos were teaching their belief that all duodenal ulcers were chronic and should be operated upon, and the whole surgical world agreed with them, I claimed in the first edition of my text book on the stomach that about one-third accomplished satisfactory results by medical means. Now I desire to raise this figure, as deducted in three hundred and twenty-four cases studied after two years of termination of treatment, to practically 50 per cent. This figure, while still not quite as high as in gastric ulcer, is high enough to warrant a trial of medical treatment in duodenal ulcer as well as in gastric.

Another point is that my experience is the same as others, in that gastric ulcer has almost no connection with carcinoma, and duodenal ulcer positively none. Here and there one has occurred but in incidence it is not even up to the medical man's allowance of five per cent. Practically all ulcers that become malignant are potentially or actually cancer with ulceration at the start. One cannot always discern this, but when a case has been on medical treatment for a month or two, as a rule, the X-ray re-examinations and checkups will tell quickly enough whether there should be a continuation of the medical treatment or a resort to surgery. What plan is simpler or more practical than this? I feel distinctly that in those patients who had an ulcer and years afterward develop a cancer, who knows whether it came from the ulcer or started independently of it? Nobody, and neither the gross nor microscopical findings can prove it.

It has been said that there are five indications for surgery, these being perforation, hemorrhage, obstruction, carcinoma, and utter failure of medical treatments. Well, I am not so sure about these as is my friend, the conservative surgeon, Dr. Frank Leahy of Boston. In perforation and carcinoma I agree totally. My attitude on frank hemorrhage has been mentioned. The recurrent type in surgical significance is often dependent upon conscientious effort in following medical treatment, how much it produces anemia, and the incidence of more frank bleedings. In certainly about a third of the cases it stops even though it had persisted for weeks or months of time. To me, the length of time of bleeding is not as important a factor for surgery as is its effect upon the body from the anemia and the recurrences of distinct bleedings.

Increasing experience- has- shown how frequently a pyloric obstruction caused by an ulcer is due to edema, congestion and interference with the normal relaxation of the pyloric sphincter. With the healing the ob-

struction often disappears. If it persists it is due to cicatricial contraction because a fibrous stricture is generally the result of many years of alternating activity and partial healing. By pyloric obstruction here is meant large retention after twelve hours, not the usual 6 or 7 hour X-ray kind. I have had not a few almost total retentions for 24 hours with enormous dilatations of the stomach and vomiting suddenly relax and the whole obstruction quickly disappear and not recur.

Regarding utter failures from medical treatment, these comprise a group of cases in which opinions must be based upon conditions concerning the patient, the type of treatment followed, and how long they were kept up. It is interesting to have operation advised because of failure of medical treatment when in reality there had been none. On this point my observations have often been about like this. An individual with a suspicion of ulcer present in the history is promptly sent for X-ray examination, nothing more being done or considered. The X-ray man reports an ulcer and then the advice is given according to the inclinations of the physician as to whether he is a medical man or a surgeon. Attitude of departmental interest in medicine is expressed which is largely personal, when it should be entirely that of the subject and patient's interest, because after all in the non-tragic ulcer case, as a rule, the patient cerebrates considerably about it, is liable to take quite an analytical interest in his ulcer, and may shop around for opinions and advice. What is especially irritating are those statements of failure of medical treatments when only an occasional dose of bicarbonate of soda had been taken. Now there is an interesting side to this that is when the surgeon himself has an ulcer, and I have seen several. He seems to care a good deal about the thing and always gives time, care, and judgment that medical procedures are given a fair chance.

Another thing I notice about the medical man when operation is contemplated on him that he is not very keen about a rather extensive partial gastrectomy being done on him. I wonder why? Great effort is being made and reasons are being given why it is the one really good thing to do. Here's my experience. If you take 100 ulcer cases you get along satisfactory well in about 75 with medical handling. In the remaining 25, the well known operations of the past will fix up about 15. About two will die from the operation, and that leaves about 8 in which the patient, the doctor, and the surgeon all together become gracefully suspended between Heaven and Earth. Some are treated medically again and an occasional one really cleans up by this combination. Some are reoperated, and I feel sorry for the surgeons in this group. Like the poor relative, they hang around. Now of course, if these are the ones who are resected—fine. But to resect in a wholesale or general way, just because an ulcer is in the stomach, had been there for some time or because surgery had failed in many cases in the past, in my opinion, never will be fair or become popular. It is a procedure for the ulcer derelicts, and with it some of these can be reclaimed. My advice in a general way with the

treatment of ulcer is to step along slowly, calmly, yet firmly. Surprises are always happening, and many of our best-arrived-at opinions are only those of conviction. Practically all of my own mistakes in cases have come when I took a definite stand and I had not had the time for good judgment, or when I did have the time, I did not exercise it. Conviction! Why? Because I still do not know what causes it.

Lambliasis Simulating Duodenal Ulcer

CASE REPORT

By Edwin Boros, M. D., *New York*

THE symptomatology of duodenal ulcer and its response to the customary medical and dietary treatment is often regarded as sufficient evidence for its diagnosis, despite the frequent absence of other confirmatory laboratory or roentgoenological data. This so-called characteristic picture of duodenal ulcer may, however, be mimicked by other conditions, one of which presented itself with a similarity of symptoms.

Mrs. H. M., married, age 43, having two children aged 18 and 14, without history of menstrual disorders or miscarriages, dated the onset of her trouble back 3 or 4 years ago, when she noticed a dirrhea as a first symptom of ill health in a past which was strikingly free from any illnesses or operations. Her discomfort was described as an intermittent watery diarrhea of one or two days duration, which announced itself as a series of cramps about the navel which soon disappeared. The infrequency of these attacks and their attribution to indiscretions of diet, relegated medical consultation to such a time, when about one year subsequently, a new series of disturbances manifested themselves, characterized by a bloating and pressure feeling in the pit of the stomach rather constant in duration. Simultaneously severe cramps about two hours after the intake of food were experienced which radiated to the right hypochondrium and back. These latter pains seem to be relieved by the application of a hot water bag and the eating of some crackers and were periodic in their occurrence. Jaundice was never observed. There was a loss of about 8 pounds in weight since the onset of the first diarrhea, despite a relatively normal appetite. The occurrence of severe cramps in the early morning hours and the failure of relief subsequent to the institution of a strict medical and dietary regimen, prompted the patient to appear, at which time she presented the following findings.

The patient was a well developed and nourished female, weighing 148 pounds, with respiration, pulse and temperature normal. The eyes, ears, nose, throat and glands revealed no disease. Examination of the chest was negative. The abdomen was scaphoid and a moderate amount of tenderness was present in the epigastrium. The superficial head zone in the right hypochondrium showed an excessive response to pressure. No mass, splenic or hepatic enlargement was disclosed, but there was a spastic cecum which rolled distinctly under the fingers together with a similar feel at the sigmoid. A gastric analysis was decided upon. The Ewald meal showed a free

acid of 35 and the total acid was 50. Fluoroscopic examination presented a hypermotile stomach with hyperperistalsis and a high secretion level. No ulcerations were found and the duodenal cap was free from any visible pathology. The blood findings were essentially negative, as was the stool. The secretions obtained by duodenal drainage dramatically demonstrated the presence of active motile forms of the Lamblia parasite, which were similarly present in the bile. Subsequent stool examinations were negative, until a fresh warm specimen finally presented active motile Lamblia.

A course of intravenous injections of .45 grams of neosalvarsan, at five day intervals was given, with an immediate amelioration of symptoms, and a total disappearance of the parasites after the fifth injection. Subsequent stool and duodenal specimens covering a period of four months failed to reveal the existence of the Lamblia, and there ensued a complete restoration to normal health.

Comment and Summary

Infection with the Lamblia parasite is apparently not as uncommon as is generally thought. Numerous cases have been reported, the first one, in N. Y. State by DuBois and Toro[1] in 1912. Chace and Tasker[2] in 1917, Kofoid, Kornhauser and Plate[3], Maxcy[4], Kennedy and Rosewarne[5] together with many other observers have called attention to the gastro-intestinal manifestations of infection by this parasite, which in man most often affects the duodenum. Their presence has been noted in the stomach when there is a diminution of gastric secretion. The gall bladder has likewise been the seat of their presence. Giardia enteritis is chronic, and the parasite has a tendency to produce considerable destruction of the intestinal mucosa. Whereas giardia has long been considered a nonpathological inhabitant of the bowel and its presence to the extent of 20% in school children without bowel disturbances has been reported by Maxcy, and in 6% of apparently healthy American soldiers by Kofoid and his coworkers, its universal distribution together with the manifold bowel disturbances attributed to its presence, should urge one to the possible consideration of its existence, which can readily be determined by the usual routine methods for examination.

BIBLIOGRAPHY

[1]DuBois and Toro: 1912 (Two cases of infection with Lamblia Intestinalis. N. Y. Pathol. Society, 12:32, 1912).

[2]Chace and Tasker: Diag. and treatment of flagellate diarrheas. Jour. A. M. A., 68:1528, May 26, 1917.

[3]Kofoid, Kornhauser and Plate: Intest. parasites in overseas, home service troops of U. S. Army. Jour. A. M. A., 72:1721, June 14, 1929.

Maxcy, K. F.: Bull. Johns Hopk. Hosp., 32:166, May, 1921.

[5]Kennedy and Rosewarne: Lancet, 1:1163, June 10, 1916.

Fantham and Porter: British Med. Jour., 2:139, July 29, 1916.

Logan and Sanfords Jour., Lab. Clin. Med., 11:618, June, 1917.

Mantovani, M.: Gazz d'osp, 40:66, Jan. 30, 1919.

Cress, W. W.: M. Recd., 98:143, July 24 1920.

Kofoid: Intest. protozoa infect in U. S. Army troops. Trans. Am. Gastro-Int. Assn., p. 262, 1919.

Congenital Obstruction of the Urinary Tract

By N. Thomas Saxl, M. D., F. A. C. P., *New York*

1. Pin Hole Meatus.

By Pin Hole Meatus is meant a very small opening at the distal end of the urethra as it emerges from the glans penis. It is rather interesting to note that this condition seems to be more familiar to pediatricians than to those in the genito-urinary field and the probable underlying reason for this is the fact that it is frequently the cause of dysuria in the male infant. Too frequently is the diagnosis overlooked and the troublesome symptoms that it causes, are wrongfully attributed to other sources.

Etiology: The stenosis is always restricted to the distal extremity of the urethra and rarely extends for more than one-third of an inch proximally. It is usually noticed between the second and the fourth year of life when symptoms become prominent, but has also been diagnosed in babies a few days old. We find it most difficult to account for this anomaly; and associated other congenital defects are rare. The urethra develops from two sources, the proximal part from urogenital sinus and the distal part is formed by the canalization of a plug of epithelium. An arrest of this latter process before a channel of adequate size has been formed caused congenital stenosis of the urinary meatus, but we do not know what factors determine this irregular development.

Signs and Symptoms: The signs and symptoms caused by this condition are two-fold: A. Those due directly to interference with the outflow of urine. B. Those due to the urinary infection which often follows this obstruction.

The commonest symptom is dysuria and the mother will call attention to the straining of the child at micturition, a small and intermittent flow associated with crying either caused directly by pain or by the anticipation of pain to come. In older children, we frequently notice an incontinence of urine which the mother claims is a frequency of micturition. These children are unable or unwilling to micturate until the bladder becomes distended and an overflow incontinence is established and a little urine dribbles away from time to time. This retention may even cause the bladder to distend up to the umbilicus and the retention becomes so acute that the patient may pass nothing for 24 hours. Further progress of this condition causes the overflow incontinence but the stagnation of the urine is frequently followed by infection and so pyuria will be the next symptom. In this effort to relieve the pain and obstruction the child frequently handles the penis and soon

superficial ulceration of the meatus may be noted. This ulcer frequently bleeds and so hematuria may be the first complaint. This ulcer is probably caused by some infected urine, that was retained proximal to the point of stenosis and actually massaged into the mucous membrane by the child's frequent handling of the penis.

Diagnosis: Pin hole meatus is frequently overlooked, but it must be remembered that phimosis per se, rarely if ever, acts as an obstruction to the outflow of urine and therefore the frequency of circumcision in these cases is to be decried. The main difficulty in diagnosing congenital stenosis of the urinary meatus is the fact that the average physician forgets that such a condition exists. A simple examination will reveal the presence of a pin hole meatus but the history of the case should make one suspect its presence even before the examination is made. The complaint of dysuria including straining and dribbling during, before and after each micturition, urethral bleeding, ulcers, incontinence of urine, frequency and bed-wetting should always lead to a most careful examination of the urinary meatus, even before any other etiological factor is considered. In rare instances, if the foreskin cannot be stretched, it may even become necessary to circumcise the boy, but if such happens to be the case, it is deemed wise to warn the parents at this time, that a second small operation may become necessary. When a clear view of the meatus has been obtained, it is usually not necessary to do more than look at it to decide whether stenosis is present or not, because, while one cannot define the normal size of the meatal orifice, nevertheless, a stenosed meatus is generally so like a pin hole, that the diagnosis is at once apparent. The technique by which one should examine the urinary meatus is as follows: Compress the meatus between the finger and thumb in the antero-postero direction (*i.e.*, in the line of the orifice) and this will show the real size of the opening. If the sides of the opening are apparently adherent this simple procedure will overcome this difficulty. Additional data and information may be gained by having the child urinate and watching the stream of urine for three factors: A. The calibre of the stream. B. Hesitancy in passing the stream. C. Interruption of the act of micturition, partially from pain.

Differential Diagnosis: Inasmuch as no other condition gives quite the same picture, the differential diagnosis should be very easy, but as mentioned above however, superficial ulcerations may give rise to bleeding. Hematuria is a common complaint in pin hole meatus, and should not be confused with hematuria from a point higher in the urinary tract. Enuresis may have various etiologies, but one should always consider pin hole meatus as a possible cause. Phimosis, as we have already noted, rarely causes an obstruction to the outflow of urine. Epispadias and hypospadias are easily recognized.

Complications: This condition, when untreated, goes on to cause back pressure and will ultimately involve even the pelvis of the kidney. Secondary infection of the urinary tract readily occurs and in some instances hydro-

nephrosis and pyonephrosis in children may be sequences of this congenital stenosis, but up to this time there is little evidence to prove or disprove this point.

Treatment: The treatment of this condition is relatively simple. Instrumental dilatation has proven to be quite unsuccessful because of the cicatrix formation that frequently follows the same. Circumcision has in all probability been unsuccessfully performed, but if not it may become necessary to do this to allow a secondary meatotomy. The results obtained from meatotomy are eminently satisfactory and permanent.

2. Congenital Obstruction in the Posterior Urethra:

Congenital obstruction in the posterior urethra is among the infrequently reported anomalies. When untreated, the patient seldom attains adult life. The efficacy of urologic treatment is entirely dependent upon the early diagnosis before grave secondary changes have taken place in the urinary organs. Disturbances of urination, pyuria, hematuria, signs of nephritis, or pyelonephritis may progressively develop and should direct attention to the urinary organs and the urological examination must be made at the earliest possible moment.

A. Hypertrophy of the Verumontanum: Bugbee and Wollstein[1] at the Babies' Hospital in New York City have given the most exhaustive report on this condition. Their report was based on 5,000 autopsies performed, and altogether totaled some ten cases. All of these, except one had been discovered at autopsy and the ages varied from thirteen days to three and a half years. In almost every instance the usual result was kidney injury and so it would seem that surgery in these cases comes too late. One patient survived 12 years and therefore a careful urologic examination is essential in these cases as soon as the obstructive disturbance manifests itself.

B. *Congenital Valvular Obstruction*: Urethral obstruction due to the presence of urethral folds that we now designate as urethral valves is not a newly discovered entity. It was first mentioned by Langenbeck[2] in 1802 and again by Velpeau[3] and Guthrie[4] in 1832. In 1891 Eigenbrodt[5] is given credit for being the first to recognize this condition in the living individual. In America this condition was first described by Knox and Sprunt[6] in 1912 and in 1913 Young[7] performed the first successful operation for its correction and was also the first observer to diagnose the condition by the use of urologic instruments ante-operatively. Hinman[8] tells us that urethral valves, while they may be regarded as rare, are frequently overlooked however.

Etiology: The location would suggest at once congenital origin. There seems to be on unanimity of opinion regarding the etiology of this condition. Bazy[9] in 1903 called attention to the fact that in the latter part of embryologic development, the urogenital membrane in the posterior urethra is to be found at the location of the verumontanum and inasmuch as congenital valves are almost always found in this location, some observers have assumed

that persistence of the membrane is responsible for their occurrence. Watson[10] believes that they appear as early as the thirteenth week and that the top of the colliculus in some way becomes attached to the roof of the urethra and it may go on for years without causing symptoms. According to Fischl's opinion a proliferation of the epithelium on the roof of the sinus urogenitalis with subsequent connective tissue adherent to the opposite wall readily accounts for the anomaly; however, none of these theories serves to explain completely all of the congenital valve formations, which have been classified by Young[7] into three types.

The first of these presents, on examination, a ridge on the floor of the posterior urethra, beginning at and continuous with the verumontanum and running anteriorly to divide at the bulbomembranous junction. The valve separating is attached as a thin membrane to the urethra in varying degrees about its circumference. In type two, the extension of the membranous sheets is posterior from the verumontanum toward the internal sphincter, where they are attached to the urethra. The third type is not continuous with the verumontanum, and may be found at any point in the posterior urethra. This variety presents the appearance of a diaphragm spread across the lumen of the urethra and pierced by a passage varying in size from pin-point caliber to a diameter which may convert the valve into an incomplete crescent, or semicircular fold on either side of the urethra. The concavity of this diaphragm is toward the bladder which allows the valve to be flattened against the urethra by instruments passed into the bladder but distends and produces obstruction when the urinary stream is directed against it.

Urethral valves are essentially a childhood disease. In the series of 56 reported cases by Hinman[8], 12 were found in the first year of life. Fuchs[12] reports a case in a five-month fetus and Schmidt [12] another in a 7-month fetus. The oldest reported by Hinman was a man of 57 and Iverson[11] reported one of 85.

Symptomatology: There is really nothing distinctive in the symptomatology of this disease. Any symptom of urinary disease such as dysuria, frequency, straining, dribbling and urgency in a very young child should make us think also of valves as a possible etiological factor. Fretfulness and restlessness usually accompanying these symptoms and persistent pyuria will undoubtedly be found. Later on evidences of back pressure with bladder distention, hypdronephrosis, etc., will be noted and as a result of this an associated pyelonephritis with renal insufficiency which terminates usually in gastro-intestinal disturbances, chills, fever and eventually uremia.

Diagnosis: With symptoms referable to the urinary tract, the diagnosis can only be made by complete urologic examination; however, physicians as a whole still present a fair amount of opposition to cystoscopy in children. This is just as easily done in a child as in an adult and there is no just cause for such an opinion. Roentgenological examination including a cystogram, revealing hydroureters and hydronephrosis (which frequently accompany valve disease) is of some assist-

ance, but when the cystogram is negative a cystoscopy must be insisted upon.

Treatment: Destruction of the valves by surgical intervention or by fulguration are the only methods advisable. The results as a rule are fairly good.

C. Dislocation of the Internal Meatus: This is an exceedingly rare type of obstruction and has been reported by Day and Vivian[12], in a case seen recently in Los Angeles. The obstruction in the posterior urethra is due to the fact that the prostatic urethra runs obliquely to one side and enters the bladder about 1 c.m. laterally to the median line. The case reported seems to be due to a malposition and overlapping of the right trigonal muscle above the left with dislocation laterally of the internal meatus and line of fusion of the two halves of the trigonal muscle. The trigone was greatly hypertrophied.

3. Congenital Ureteral Obstruction:

A. Strictures: These lesions account for more than half of all ureteral obstructions. These strictures show a very definite predilection for the ureteral extremes, *i. e.*, the pelvic or vesical insertion. However, they may occur at any point along the course of the ureter and may be single, multiple, unilateral and bilateral. Some observers consider these obstructions as mucosal redundancies with valve formation and there is no question of doubt that this is true in many instances; however, histologic examination of these lesions reveals marked mural fibrosis.

B. Kinks: The usual site is near the ureteral pelvic junction, but may occur at any point along the course of the ureter. Campbell[13] cites a case in mono-ovular twins in which autopsy revealed sharp "S" shaped kinkings in the left ureters at precisely the same point. He further mentions as a curiosity that there were also identical transduodenal bands. However, congenital kinks are exceedingly rare.

A case that illustrates congenital ureteral obstruction (see figure 1) was that of J. M., a boy of four months who was brought to the Post Graudate Hospital on December 23rd, 1929, with the complaint of fever and vomiting of about four days duration. Physical examination showed contracted pupils, reacting sluggishly to light, stiff neck, Kernig and Brudzinski. Spinal tap showed turbid fluid, 4150 cells, 91% Polys, +++ Globulin and culture later showed meningococcus. Serum treatment was instituted and continued until fluid was clear and cells down to 30. Stiff neck remained. Child did not pick up, but continued on a downgrade. Frequent taps showed no marked evidence of further pathology. About January 7th, fifteen days after admission, suspicious signs of pneumonia in the right lung appeared and the patient's temperature which had returned to normal now rose again and continued high with occasional remissions. One day later the signs of pneumonia in right chest became conclusive and x-ray showed further evidence. On January 16th, eight days later, the right chest showed signs of consolidation in upper, middle and lower lobes posteriorly and in the axilla. The patient died on January 16th, and autopsy revealed the following:

1. Subacute fibrino-purulent meningitis.

2. Right interstitial broncho-pneumonia with atelecasis, fibrinop urulent pleurisy and empyema.

3. Vesicular and ulcerative infection of skin, especially neck and scalp.

4. Punctate hemorrhages of gastric mucosa.

5. Dilation of right heart.

6. Acute passive congestion of abdominal viscera.

7. Congenital aplasia of left kidney, with compensatory hypertrophy of the right.

8. Left hydroureter and hydronephrosis.

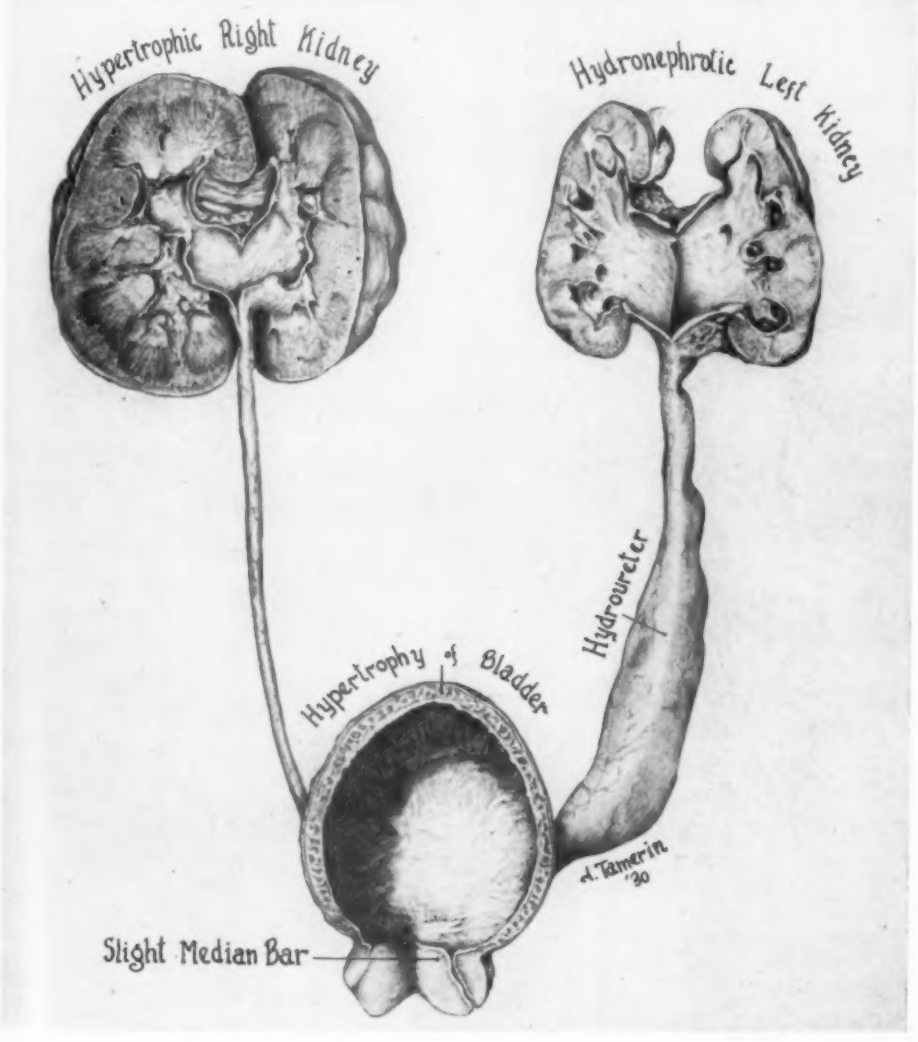

FIG. 1

9. Hypertrophy of urinary bladder walls.

10. Congenital vulvular stenosis of left ureteral meatus.

11. Phimosis.

4. *Median Bar*: Some authors believe that the so-called median bar is not congenital, but is caused by chronic inflammation. Pugh[15] says that it is undoubtedly a sequel of an old gonorrhea. He feels that a very small percentage of our gonorrhea patients are cured and the disease remains in the deep urethra and that during the course of years, an inflammatory condition extending from the prostate up into the vesical sphincter forms a very definite bar or ridge. These bars may simulate small median lobes or may gradually extend completely around the vesical neck forming a true collar obstruction.

On the other hand, there are those of us who feel that in addition to this type of median bar, there also exists another form which is congenital in origin as can be seen in the following case: (figure II)

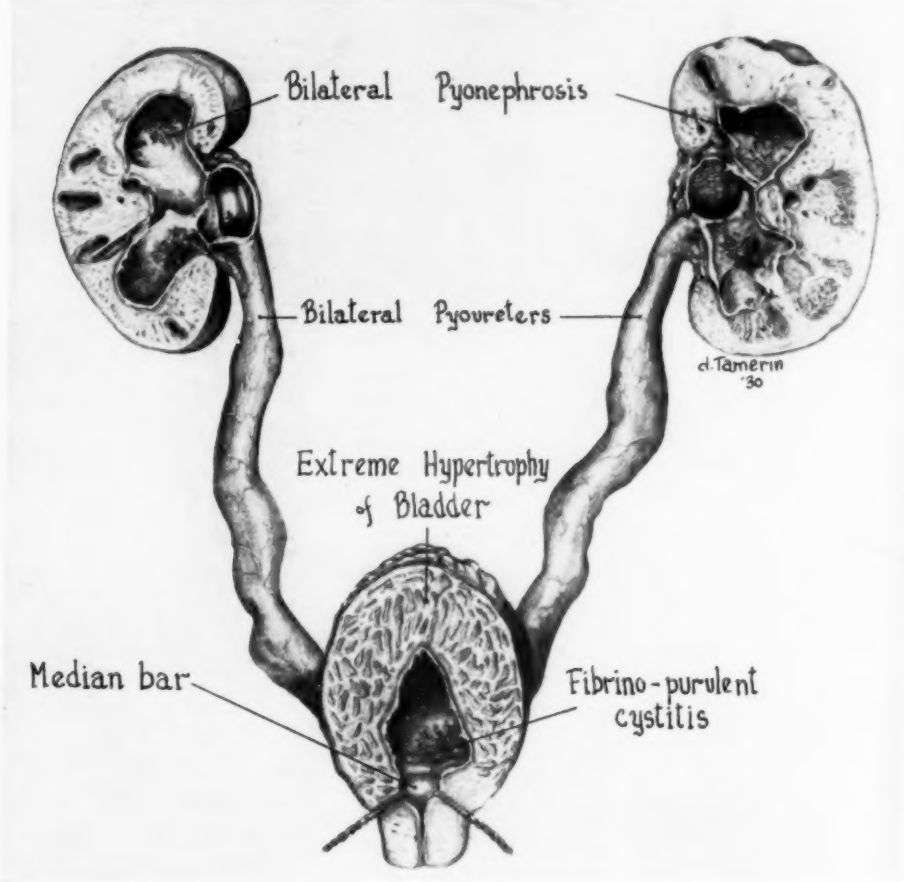

FIG. 2

F. N., age 15 days, admitted to the New York Post Graduate Hospital on September 12th, 1929, with a chief complaint of scrotal swelling apparently since birth. This had begun to increase in size during the 24 hours before admission so that (according to history) there had been retention of urine. This however, was not substantiated as patient voided while in hospital. The scrotal swelling increased and the penis become quite edematous. The child's general condition was more serious than the local condition would account for. White blood cells were 34,000, the urine was loaded with pus and red blood cells. A dorsal slit was done, and a large amount of pus was obtained from scrotum. The patient died the following day. Autopsy revealed the following:

1. Acute pyelonephritis.
2. Acute fibrinous peritonitis.
3. Acute fibrinopurulent cystitis.
4. Peri-urethral abscess.
5. Surgical incision of scrotum.
6. Hypertrophy of bladder.
7. Congenital Median Bar.

REFERENCES

[1]Bugbee, H. G., and Wollstein, Martha: J. Urol., 10:477 (Dec.) 1923.

[2]Langenbech, C. J. M. Wurzburg: Stahel; 1802, XXVI., 71 p. 6 pl. 4[1].

[3]Velpeau: Paris, Jr. B. Bailliere, 1832, 3 V. 8°, Atlas 4°.

[4]Guthrie, G. J., London, Burgess and Hill: 1834, 1 L. 284 p. 3 col. pl. 80.

[5]Eigenbrodt: Beitr. z. klin. Chir., 8:1711, 1891-1892.

[6]Knox, J. H. M., and Spruit, T. B.: Congenital Obstruction of the Posterior Urethra, Am. Jour. Dis. Child., 4:137 (Sept.) 1912.

[7]Young, H. H.: Practice of Urology, Philadelphia, W. B. Saunders Company, 2:93, 1926.

[8]Hinman, F., and Kutzmann, A. A.: Jour. Urol., 14:71 Aug. 1925.

[9]Bazy, L. V.: Paris, C. Laud. 1903, 22 p. 8°, Extrait La Presse Medicale, Mar. 7, 1903.

[10]Watson, E. M.: 11 p. 120, Repr. Med. Rec. Oct. 6, 1917, also Repr. Trans. Sec. Urol. A. M. A., 1921.

[11]Iversen, A., Kjbenhaver, G. E. C.: Gad., 1876, 155 p. 8°.

[12]Day, Robert V.: Los Angeles, Vivian, Charles S., Phoenix, Ariz.: Congenital Obstructions in the Posterior Urethra, Sec. Urology, A. M. A., 1927.

[13]Campbell, Meredith F. and Lyttle, John D.: Ureteral Obstruction in infancy, Jour. A. M. A., Vol. 92, No. 7, Feb. 16, 1929, p. 544.

[14]Lloyd, E. I.: Treatment of Congenital Stenosis of the Urinary Meatus, The Lancet, Dec. 10, 1927.

[15]Pugh, W. S.: Urinary Obstruction, Surgical Clinics of North America, P. 283, April, 1028

Psychiatric Consultation Service Supplied by the State Department of Health

By James L. McCartney, M. D., *Chief, Division of Mental Hygiene, Connecticut State Department of Health, Hartford, Conn.*

At present thirty-eight states in the Union have some form of Mental Hygiene and Psychiatric Consultation Service. In these states there are eight hundred and fifty mental hygiene clinics,[1] dealing with neuro-psychiatric problems of the adult and child. Most of these organizations are privately endowed, there being only ten states which furnish these facilities through the State Department. Only one of these ten states definitely ties up psychiatry with the general health problem, this state being Connecticut, which has mental hygiene as an intrinsic part of the State health program.

Preventive medicine has become an established fact. It is now more than thirty years since the prevention of tuberculosis has become an important link in the chain of protective services, designed to control disease. At present there are about six hundred clinics for tuberculosis in operation in the United States and this number seems adequate. There are some eight hundred venereal disease clinics supplying the need in that field reasonably well.[2] Yet, it is evident that the eight hundred and fifty neuropsychiatric clinics mentioned are quite definitely insufficient for more than a small fraction of the need in our present social system.

The First International Congress held in Washington this last May brought out the fact clearly that mental hygiene is of paramount importance in any general health program. This need is realized when it is found that there are more patients in mental hospitals than there are physically-sick patients in the general hospitals of the whole country, and the mental hospitals are at all times so overcrowded that many needy cases are denied admission. The preventive angle of this problem is significant since at least half of all cases of mental and nervous disorders can be prevented by the timely application, largely in childhood and adolescence, of available knowledge. Every general physician is faced with the problem of handling these neouropsychiatric cases but he usually finds himself without the necessary knowledge to give the adequate treatment.

When a full-time Division of Mental Hygiene of the Connecticut State Department of Health was established, it was found that there was a need and a demand for a Consultation Service in Mental Hygiene and Psychiatry, which might be available to physicians and social agencies, who were frequently faced with personality

problems. Unfortunately, there is an inadequate supply of private psychiatrists to handle these cases, and few of these psychiatrists maintain a clinical set-up. Consequently, this service was made available and is furnished gratis to all recognized physicians in the State as well as to all organizations working in co-operation with such physicians. All nervous and mental problems may be referred for diagnosis and advice as to treatment. Persons of both sexes and all ages are examined, and although no treatment is given, whenever possible, a detailed outline of treatment is sent back to the referring party, and the patient advised to follow his advice.

During a period of seven months (October 1929 to May 1930) two hundred and twenty-six cases were referred to the Division of Mental Hygiene for examination, and of this number 52 per cent were boys under eighteen, 23.5 per cent were girls, 11.5 per cent were men and 13 per cent women. Of the total number referred 17 per cent were directly from physicians, 63 per cent from visiting nurses and school nurses, 7 per cent from State agencies, and 13 per cent from private social agencies.

When consultation is desired the accompanying form is filled out and returned to the central office at least two weeks before the time set for consideration, and in only emergency cases is this rule departed from. This period of two weeks allows time to make a careful, social study of the patient's background and environment, which is very necessary for an intelligent examination of the patient.

In making a psychiatric examination, it is necessary to study the individual as a whole. Fortunately, practitioners are more and more realizing the necessity of considering all types of patients in this light. In attempting to interpret deviations of character this is obviously important, for in studying behavior many persons may be involved. Parents have to be reckoned with in studying their children, teachers in their pupils, and employers in their workers.

In order to study the patient as a whole a four-fold examination should be made and every consultation service handling neuropsychiatric cases should

REFERENCE BLANK

(Fill in by typewriter or printing)

NAME — DATE OF BIRTH

ADDRESS — PLACE OF BIRTH

SCHOOL GRADE OR EDUCATION — SEX — COLOR — RELIGION

OCCUPATION

REFERRED BY: — ORGANIZATION OR ADDRESS

PARENTS: FATHER — ADDRESS AND OCCUPATION

(Name and Age)

MOTHER — ADDRESS AND OCCUPATION

BROTHERS AND SISTERS (In order with addresses)

REASONS FOR REFERENCE

INTERESTED PERSONS AND AGENCIES

PHYSICAL CONDITION

REMARKS

have the standard mental hygiene set-up composed of a psychiatrist, who, of course, is a physician to begin with, and who should be well versed in general diagnoses; a psychologist, who has been trained in the testing of intelligence; and a psychiatric social worker who has had a thorough training in case history taking. It has usually been found that for every psychiatrist, a half-time psychologist, and two or three psychiatric social workers are necessary to conduct a full-time program.

To obtain an adequate idea of the patient's background, the psychiatric social worker should trace the development of his habits, particularly if they are abnormal, and the companions he selects should be ascertained, to see if there is any apparent ill effect they may have upon him. It is also necessary to know how he uses his spare time, what recreation he chooses, his interests, and where they take him. The stages by which his misconduct has grown, its early beginning, and the facts surrounding them, are important in outlining treatment. His mental accomplishments have to be accurately evaluated and a full school history which portrays both his failures and his successes must be obtained. His past ill-health may be a factor, and this must be investigated. It is also very necessary to know the circumstances of the child's conception and birth. In other words, a well-trained worker will trace in detail the development of the patient's personality. Commencing with his hereditary predisposition, she will follow step by step all the important factors until a well balanced picture is drawn. This of course necessitates a detailed family history, and all this hereditary data should be gathered with insight. "Her story should give the information as to how his ancestors dealt with their life situations —whether they were able to meet reality or whether they were 'routed and fled',—whether grandfather could face the responsibilities of an ever increasing family or whether he 'deserted the ranks', cutting himself off from the family, perhaps hiding behind an effective barrier of irritability or anger, or 'buried his head in the sand' by imbibing alcohol too freely"[8].

Scientific work of the last few years has demonstrated with new thoughtfulness that mind and body are inseparably joined together,—that abnormal mental states affect physical health, and abnormal physical states affect mental health. The mind is the correlator of all the various functions and processes of the body. If the examiner is to have a well-rounded idea of the patient's problem, he must know of his physical health. Every resource of modern medicine should be considered in the examination of the patient, for it is seldom that some form of medical care is not necessary in the treatment of these patients, often times these points being missed by the general physician, although important and significant in the consideration of the total personality. It is important to ascertain whether it is eyestrain, malnutrition, flat feet, or other defect that is producing the increasing irritability, and obviously the trouble must be corrected if the patient's behavior is to be improved. Marked feelings of inferiority nearly always accompany physical defect, and personality diffi-

culties often result from abnormal functioning of the ductless glands. Not infrequently an apparently reckless, hyper-active, troublesome person will prove to be a seriously fatigued individual whose fatigue has become a chronic state. He is too uneasy to keep still, continually "on the go" and he may try to relieve his discomfort by seeking excitement. Some of the so-called bad boys will prove to be early cases of tuberculosis. In all of the cases of speech difficulty frequently referred for psychiatric consultation, it would be absurd to try to make a diagnosis without a complete physical examination. It is thus evident why the Health Officer or the family physician is asked to make a detailed physical examination, and to send in their report previous to the psychiatric examination, and if possible, at the time of reference. Where it appears necessary, an X-ray, serological or basal metabolism test may be requested.

A well-trained psychologist can give valuable information concerning a person's ability and thus in the consideration of many juvenile problems, it is necessary to have a thorough psychological and educational examination given as routine. The patient is first given a test to determine the quantity of his intelligence, the result of these tests being expressed in terms of mental age. If, for example, his score shows a mental age of 12 years, it means that he has the same quantity of intelligence as the average child of 12 years. When his mental age is compared with his actual life age, some idea is gained of the comparative quantity of his intelligence compared with other children of the same life age. This comparative quantity is generally expressed in terms of percentage and is called the child's Intelligence Quotient, or his "I.Q." Generally speaking, children with an "I.Q." of from 90 to 110 are considered to have a normal quantity of intelligence, while those below these figures are sub-normal, and those above are superior. The "I.Q." should never be interpreted without an adequate social history, a complete physical examination and a thorough psychiatric examination. Emotional factors may enter into the result of an individual test so that gross injustice and real harm may be done.

In addition to the intelligence test, the clinical psychologist should give a performance test, which is important, especially in dealing with the question of vocational guidance. If possible, the child should also be given an educational test. The test of intelligence shows the child's native or potential ability but the educational test shows to what purpose he has used these abilities. The result indicates what he has accomplished. His abilities and accomplishments can now be compared. This comparison is again expressed, in terms of percentage and is called the accomplishment ratio. In this manner, at times, a dull child is found to have made better use of his intelligence than some very superior children, and this may give insight into some of his other traits or tendencies.

In the social history, it is important to ascertain what the persons in the patient's environment think of him; in the medical examination, what the physician thinks of his body; and it is important to know what the psychologist has discovered about his

mental equipment, but it is the problem of the psychiatrist, to ascertain what the person thinks about himself, how he feels towards those in his environment, what he thinks of the world and life in general, his parents, his marriage partner, his home, his brother and sisters, and his conduct towards them. If he has been an unwanted child, how much more critical would his parents have been towards him; his simple childlike mischievousness being interpreted as innate perversity. The psychiatrist endeavors to discover what mental twist is causing the disorder. His experience with abnormal mental states gives him the technique and insight. His study of these disordered minds throws much light on normal mental mechanisms. The psychiatrist as stated above, is primarily a physician, and it is as one who heals the sick that he views the problem child or the problem adult.

In the Consultation Service as furnished in Connecticut, after the examinations as listed above are completed, the facts are all gathered together, digested, and an attempt is made to diagnose the case, and treatment is then outlined. When a case is referred for consultation, a careful study is made of the local facilities for caring for neuropsychiatric cases, the schools and institutions are visited and influential citizens are interviewed, so that these individuals may be enlightened and may be better prepared to accept the recommendations that may have to be made, which at times are rather of a radical nature. Where ever possible, the referring party is interviewed and the cases are discussed in detail, so that there may be no misunderstanding. As in the examination, the treatment of most neuropsychiatric cases does not fall on one person, but included the patient, his parents, his associates, his teachers, employers and the clinician who referred the case, all of whose attitudes, many times, need changing. This may be the most important part of the treatment.

Of the 226 cases seen in consultation as before mentioned, the diagnoses were as follows:

	No. of cases	Percentage
Psychoses	11	5.0
Psychoneuroses	20	9.0
Neurological problems	38	17.0
Emotional problems primarily on a physical basis	23	10.2
Habit disorders	11	5.0
Personality difficulties	15	6.6
Behavior problems, not referred through courts dependent on:		
Mental Defect	8	3.5
Mental Superiority	2	0.8
Environmental handicaps	38	17.0
Emotional instability	14	6.2
Other factors	6	2.6
Problems of Delinquency referred by courts, dependent on environmental handicaps	2	0.8
Intelligence Problems:		
Superior Intelligence	6	2.6
Borderline Intelligence	9	3.8
Feeblemindedness	23	10.2
	226	

This Consultation Service in Connecticut has been carried on as only one of the numerous duties of the Division, so that the time available has necessarily been limited and it has been found that the demand has been far beyond our facilities. A social examination of a case involves at least two hours of a social worker's time, many times requiring as much as half a day; while a psychiatric examination, in most cases, has required at least an hour. Although we have found many cases in which we have felt that it would have been advisable to have spent even more time than this, the demands on our service have been such that many times we have cut down our time scheduled for certain cases to less than an hour.

It will be concluded from what has been said before that in psychiatric consultation work, possibly more so, than in any branch of diagnoses, a "snap" diagnosis cannot be made, as no two people are alike, and so no two cases are alike. Each case has its own individual causative and associative factors, so generalizations are almost impossible and extremely dangerous. It is seldom that factors needing correction are not found in all four fields listed above,—social, physical, psychological and psychiatric. Anything less than a complete study is very risky and may prove fearfully damaging. Each individual under examination must be considered a personality, if he is to be guided and helped to an adjustment of his emotions.

[1]List of Psychiatric Clinics in the United States: Children's Bureau-Publication No. 191, United States Printing Office, Washington, 1929.

[2]Emerson, Haven: The Magnitude of Nervous and Mental Diseases in a Public Health Problem, Proceedings of the First International Congress on Mental Hygiene, May 6, 1930.

[3]Emery, E. Van Norman: The Child Guidance Clinic, Pamphlet of the National Commitee for Mental Hygiene, 1926.

Experimental Studies of Nerve Impulses*

An Attempted Correlation Between Physiology and Symptomatology

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THE list of independent observers who have recorded the arrest of remote dysfunctions by the interception of nerve impulses passing the sphenopalatine ganglion[1, 2, *] has become so extensive, and the number of instances so great that it may seem a threshing out of old straw to emphasize the causal relationship involved. It is the mechanism which challenges inquiry. However, analysis of the mechanism is best begun by a careful scrutiny of the factual basis and the logical groundwork.

That these phenomena could be interpreted as due to systemic action of the drug or to psychic reaction of the patient may be dismissed without comment. Even to raise such questions would be to proclaim an unfamiliarity with the field of observation—they are too easily answered by simple tests.

As early as 1908 Ewing[3] arrested eye pain (glaucoma) by anesthetization of the sphenopalatine ganglion. The observation that such arrest of pain is not accompanied by any detectable anesthesia of the eye has since been corroborated by other observers[1] and has been well demonstrated in traumatic ulcer of the cornea, the exquisite pain of which may be arrested while the injured cornea remains as sensitive to the touch of a wisp of cotton as its fellow of the opposite side. Moreover it has been shown[1] that if the arrest of pain obtained by anesthetization of the sphenopalatine ganglion resulted from the interception of the *pain message* then whenever the ganglion is anesthetized all the major regions of the body (where

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*It should be noted that no dysfunction has been found, all cases of which are arrestible by this procedure. Although it has not yet been possible to subject to statistical analysis the proportion of cases thus relievable through the list of some seventy dysfunctions now recorded, it may nevertheless be observed that this ratio is quite variable in one dysfunction as compared with another. For example, in lumbago an ample majority of cases are relieved, and in most of these cases the relief lasts indefinitely, while in sciatica and many other dysfunctions only a minority of cases respond—perhaps a fourth or a fifth, and in these the relief is a little less likely to be permanent. Since some cases of so many maladies are relievable, however, the procedure is one of large therapeutic value.

dysfunctions may potentially be relieved) would be involved in a widespread anesthesia, and when the ganglion is injected with alcohol this anesthesia would persist for several months, which is not found to be the case at all.

Also it is observed that anesthetization of the sphenopalatine ganglion may arrest dysfunctions of other categories than sensory, as motor, secretory, respiratory, circulatory and endocrine, and that a single anesthetization may arrest both sensory and motor, or sensory and secretory, or motor and secretory dysfunctions, and so on in varying combinations. Findings of this kind seem to demand that the phenomena be accorded a unity of interpretation, and that an explanation that is not equally tenable for the whole aggregate be not accepted.

The demand for such an explanation suggests that we turn to physiology. Our own endeavors to obtain a physiologic explanation of these phenomena have been continued over a number of years. Among those consulted in this country and abroad was Howell, of Johns-Hopkins, who said: "There is nothing known in anatomy and physiology that provides a rational basis of interpretation for the results that you claim."

If the fact that asthma, chorea or diarrhea may be arrested in certain cases by anesthetizing the sphenopalatine ganglion is at variance with the present day teachings of physiology, the variance cannot but require some modification of our physiological conceptions, since in science the observed facts make up the environment to which theories must adapt themselves if they are to survive. The object of this paper is to suggest that the variance may be more apparent than real, and that through correlation of physiologic principles already at our disposal, it may, perhaps, disappear.

Nerve Impulses* an Essential Factor in Causation of Symptoms

It is observed that the arrest of dysfunctions may be effected through anesthetization of the strategic sphenopalatine ganglion (right or left as the case may be) (a) by topical application of cocaine or butyn, (b) by the injection of alcohol into the ganglion, or (c) by the injection of novocain into its immediate environs. From this it is concluded that the arrest of the sympton *is effected by virtue of some action that these four procedures have in common.* It cannot be anesthetization of the nerve, for alcohol does not anesthetize the nerve but destroys its fibers, nor can it be destruction of the nerve fibers, for cocain and butyn do not destroy the fibers. They all, however, have one effect in common, namely, *to prevent the passage of nerve impulses over the treated section.* It is therefore concluded THAT NERVE IMPULSES ARE AN ESSENTIAL FACTOR IN THE CAUSATION OF THE SYMPTOMS THUS ARRESTED.

Arrest of Dyspnea by Intercepting Impulses on Vidian Nerve

In the foregoing clinical investigations, 1, 2, the dysfunction could

*The term *impulse* is used instead of *current*, not because it more accurately represents our conception of the entity, but out of deference to the language of physiology.

be made the subject of experimental inquiry only after it had occurred spontaneously in a state of nature. By the manner in which it was arrestible we might infer its causation, but we never directly caused it. In the following the dysfunction was not merely arrested at will, but precipitated at will as well. The experiments to be presented as illustrative of this group are based upon the relationship between nerve impulses and asthmatic dyspnea.*

Experiment 1, May 8. (Case of Mrs. M., for 17 years a sufferer from paroxysmal dyspnea.) During an attack of paroxysmal dyspnea the right sphenopalatine ganglion was anesthetized.* The dyspnea ceased completely within less than give minutes.

*Although the diagnosis of asthma made by the various physicians through whose hands these patients have passed seems to be correct, inasmuch as this is a study of nerve impulses rather than of symptomatology, our concern being not with the nature of the symptom but with the consistency of its reaction to our tests, the more general designation, *dyspnea,* has been chosen.

While more than a hundred cases of dyspnea have been tested by anesthetization of the sphenopalatine ganglion during the attack, in only twenty-four of them has the attack been arrested. It is significant that of these twenty-four, not one has been relieved by anesthetizing the sphenopalatine ganglion of the left side—all were from the right.

*Technic of anesthetization: Two drops of 50% butyn on a pledget of cotton previously moistened with 1/1000 adrenalin, placed against the wall of the nasopharynx just posterior to the tip of the middle turbinate. This technic has been standardized, and will henceforth be designated simply as anesthetization of the sphenopalatine ganglion. For details see J. Mich. St. Med. Soc. 29:294, April, 1930.

The situation would seem to be analogous to that in the laboratory experiment in which the vidian nerve is sectioned at its junction with the sphenopalatine ganglion, and the distal end stimulated.*

Etiology Not Attributable to the Ganglion

We do not wish to convey the impression that the impulses involved originate at the sphenopalatine ganglion, or indeed, that this ganglion has any part to play in the etiology of these cases. It is believed that the ganglion is not usually an etiological factor at all, but serves merely as a medium of conveyance for the actuating impulses. The following case, observed in 1926, and a number of similar ones that could be cited, tend to discredit the supposition that the ganglion itself is an etiological factor.

Miss J. B., age 30, had been a sufferer from asthmatic dyspnea for a

*Nearly two years ago the writer, visiting the physiologic laboratories of one of the great institutions of the middle West, witnessed the following experiment: Where the sphenopalatine ganglion and the vidian nerve in an animal had been exposed, a stimulus was being alternately applied to the vidian nerve and withdrawn. When the stimulus was applied, the respiration, heart action and blood pressure became quite disturbed; when withdrawn, these disturbances would subside. We are here reminded that the capacity of nerve impulses to cause dysfunctions is continually employed in the conduct of experiments in the physiologic laboratories. Physiologic research, indeed, would be greatly handicapped without it. An anomaly is that this fundamental physiologic principle seems never to have been correlated with symptomatology, or to have been applied, to any appreciable extent, in the practice of medicine.

number of years, when it was found that anesthetizing the right sphenopalatine ganglion in mid-attack gave prompt and complete, though temporary, relief. This test was repeated on many occasions over a period of three months, always with uniform results. At length the right sphenopalatine ganglion was injected with alcohol, whereupon the dyspnea ceased. The patient continued free from the affection for six weeks, at the end of which time the dyspnea suddenly returned with all its former severity.

This raised the question whether the injection had been faultily placed, in consequence of which its effects were prematurely gone, or whether some other factor had intervened. It was expected that if the return of the symptoms were due to faulty and short-lived injection, then anesthetization of the ganglion would again relieve the dyspnea, as it had before. In such tests, however, it was found that anesthetization of the ganglion now would not relieve the dyspnea in the slightest.

Conclusion: The alcohol injection was still in effect, and the sphenopalatine ganglion was now not even playing a passive role in the etiology of the dyspnea; otherwise its anesthetization would have arrested the symptoms. It would seem that when the ganglion was injected with alcohol, the nerve impulses actuating the dyspnea were more or less permanently intercepted, and that for a time this prevented the recurrence of the malady. But at the end of six weeks, while the ganglion was still impervious to the passage of impulses, *some change supervened*, resulting in the return of the symptoms in spite of this obstruction.

The question now arises, what was this sudden change, permitting the dyspnea, formerly arrested at the ganglion, to return with the ganglion still blocked? Was it simply the routing of the actuating impulses that had changed—a detouring of the obstructed ganglion? Apropos, that nerve impulses do have alternative routings to which they may be diverted according to the resistance encountered, we have no less authority than that of Ranson.[4]

The thought that there may be a considerable diversity of routing of nerve impulses is a very fruitful one. It would account as well for the numerous cases in which the dysfunction is not arrestible at the sphenopalatine ganglion at all, as for cases like the preceding, in which the ganglion, after a time, ceases to be strategic.

Relevant Principles of Anatomy and Physiology

Although our experiments have indicated that nerve impulses are capable of causing dysfunctions, and although in certain cases studied we find evidence of these impulses moving over the vidian nerve in a direction away from the sphenopalatine ganglion, still it is to the fundamental principles of anatomy and physiology that we must turn for a larger conception of the factors involved. From anatomy we learn that the structural unit of the nervous system is the neuron, that is, the nerve cell with its processes. In the words of Ranson[4] "These cellular units remain anatomi-

cally separate, i.e., while they come into contact with each other at the synapses, there is no continuity of their substance." From physiology we learn that whatever the nerves do, they do by means of impulses or currents sent along their course. It is these impulses that make the muscles contract, the glands secrete, the heart beat faster or not so fast, that convey messages, as of sensation, pain, emotion, thought—in fine, it is by means of these impulses that we live and move and have our being.

Learning from physiology that the active constituent of the nervous mechanism is the impulse, without which the organism could not maintain its functions, simplifies our thought processes. Visualizing the nerve impulse as being passed from neuron to neuron, as a ball is passed across the field from player to player, we are relieved of the necessity of thinking in terms of a complex "wiring system" and may think in terms of the impulses moving over that system. No less clarifying to our thought processes is the conception, well expressed by Ranson, that nerve impulses have a variety of alternative routes which are taken according to the resistance encountered.

Physiology offers us even further help, however, for we are taught by Howell[5] that efferent impulses flow out from the brain "in a more or less continuous stream" to "motivate and stabilize" the various physiologic functions, while from Sir Arthur Lovatt Evans[6] we learn that the transition from function to dysfunction is quantitative. "A state of disease is never a thing in itself, but is always a quantitative change in some physiological process, an increase or diminution of something that was there to begin with."

Reflection on these basic principles can hardly fail to bring us to the conclusion that efferent impulses must not always be distributed in the right quantum, since every mechanism is subject to imperfections, and that efferent impulses distributed in sufficiently abnormal quantum must result in dysfunction. For example, in an eye with poor drainage, efferent impulses reaching the ciliary body and iris in excess might over-motivate the intraocular secretions as to cause a rise in intraocular tension, thus producing the dysfunction we know as glaucoma. Similarly efferent impulses in excess reaching the musculature of the arterioles might unduly contract them, producing, if the contraction was general, hypertension, or if local, Buerger's disease or Raynaud's disease.[7] Reaching other muscles, such excess impulses might produce cramps or spasms, as spasm of the esophagus, observed by Sluder,[8] or bronchiospasm, or asthma.[1,9] Upon reaching the motor terminals of a striated muscle, such excess impulses, if more or less continuous, would be expected to produce spastic paralysis,[10] or if intermittent and incoordinated, chorea.[11] In the secretory glands of the intestine they would be expected to produce diarrhea,[8] in the thyroid, hyperthyroidism.[1]

Conclusions

1. The arrest of dysfunctions by anesthetization of the sphenopalatine ganglion is not to be interpreted as the

result of any systematic action of drugs or psychic reaction of the patients.

2. The perception of pain might be arrested by interference with either the *cause* or the report to the center of consciousness—the pain message. It is demonstrable that our results are not achieved by intercepting the *pain message* (a) because anesthesia is not detectable in the erstwhile locus of distress, (b) because the widespread anesthesia involving head, neck, trunk and extremities which such an interpretation would postulate whenever the ganglion is anesthetized is not found to exist, and (c) because not merely subjective but *objective* dysfunctions, such as dyspnea, chorea, diarrhea and hypertension may be arrested by anesthetization of the sphenopalatine ganglion.

Experiment 2, May 12. In the same case ½ cc. 1½% novocain was injected into the right sphenoid sinus. The dyspnea was again arrested within less than five minutes.

Experiment 3, May 27. With a 10 cm. needle, slightly curved at the tip, ½ cc. 1½% novocain was injected as far back and as far lateral as possible beneath the sphenoid sinus, near the path of the vidian nerve. Again the dyspnea was immediately arrested in mid-attack.

Up to the present time (July 10) the dyspnea has continued to be arrestible in mid-attack at any one of these three points, as follows: By anesthetization of the right sphenopalatine ganglion, by injection of anesthetic solutions into the right sphenoid sinus, and by injection or topical application of anesthetic solutions beneath the sphenoid sinus along the path of the vidian nerve.

Conclusion: Confirming Sluder's observations, made as far back as 1912, that anesthetic solutions may act through the bony tissues of the vidian canal, these experiments demonstrate the arrest of dyspnea by the interception of nerve impulses passing over the vidian nerve (a) at its extremity in the sphenopalatine ganglion (point 3 in figure,) and (b and c) at points along its course through the floor of the sphenoid sinus (points 4 and 6 in figure.)

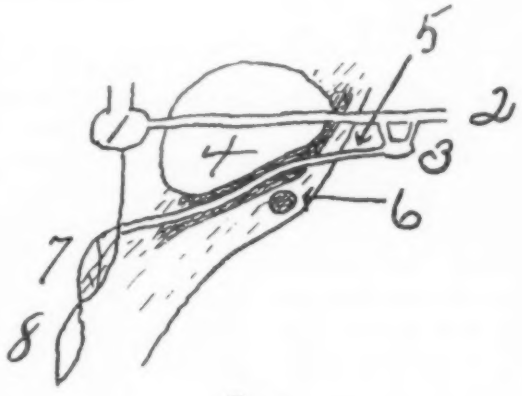

FIG. 1

Causing Dyspnea at Will Direction of Impulses

While the above experiments indicate that the passage of impulses over the vidian nerve was an essential factor in the causation of the dyspnea, they do not give us the direction in which such impulses were moving—a point on which the following experiment may perhaps throw some illumination.

Experiment 4, May 23. (Case of J. G., for 15 years a sufferer from paroxysmal dyspnea.) The patient came in free from dyspnea, but a mild farradic current applied to the sub-sphenoid region (point 6 in figure) brought on an attack, which continued after the stimulus was withdrawn. The right sphenopalatine ganglion was now anesthetized, whereupon the attack was immediately arrested. After this had been done it was found that farradic stimulation of the vidian nerve would still bring on the symptoms, but they would subside promptly as soon as the stimulation ceased.

Experiment 5, May 30. In the same case it was found that stimulation of the sphenopalatine ganglion would bring on the dyspnea when the vidian pathway was open, but would not after the vidian nerve had been blocked. That the stimulus was actually reaching the sphenopalatine ganglion was indicated by the paresthesias obtained in the sphenopalatine distribution.

Conclusion: These tests would seem to indicate that the impulses producing the dyspnea were passing over the vidian nerve in a direction away from the sphenopalatine ganglion instead of toward it, as some have supposed.

3. The fact that the arrest of dysfunctions may be effected by the use of cocain, butyn, novocain, or alcohol indicates that it results from the one property which these four have in common: the interception of the passage of nerve impulses. *In other words, nerve impulses are an essential factor in the causation of these dysfunctions.*

4. That nerve impulses are capable of causing dysfunctions, it is noted, is a principle continually employed in the physiologic laboratory as an incident to numerous experiments.

5. Our own experiments with nerve impulses, by which we not merely arrest a dysfunction at will, but provoked it at will also, give further evidence that nerve impulses may cause dysfunctions.

6. That we have been able to provoke dyspnea by applying a stimulus to the vidian nerve while its terminus at the sphenopalatine ganglion was blocked indicates that the direction of these impulses over the vidian is not toward the sphenopalatine ganglion, but the opposite toward the carotid plexus.

7. From the correlation of two fundamental principles of physiology (the principle that the organism is motivated by efferent impulses and the principle that the transition from function to dysfunction is quantitative) we are led to the conclusion that efferent impulses are expected to be sometimes distributed in abnormal quantum, dys-stabilizing functions and converting them into dysfunctions.

Comment

Perhaps the *nerve impulses* of the clinic, the *efferent impulses* of physiology, and the *electric energy* of the bipolar theory may ultimately be identified as a single entity.

The bipolar theory, which postulates that the nerves serve, not merely for the transmission of messages but for the distribution of energy, and the findings of the clinic are strikingly in accord. Evidence that the nerve currents investigated in the clinic not only motivate and dysmotivate functions, but are *capable of traumatizing the cells themselves,* is reserved for treatment in a subsequent paper. For the present it is sufficient to show that these currents, which are capable of *causing* pain, *are not pain messages.* The fact that these currents actuate motor, secretory, and other energy manifestations suggests that their study may not only bring about a correlation between symptomatology and physiology, but may integrate the work of the clinic with that cosmic energy conception of living processes, the bipolar theory.

BIBLIOGRAPHY

[1]Byrd, H. and Byrd, W.: Sphenopalatine Phenomena, Present Status of Knowledge of. Arch. Int. Med. (in press.)

[2]Byrd, H. and Byrd, W.: Sphenopalatine Treatment in Affections of the Trunk and Extremities.

[3]Ewing, A. E.: Pain of Acute Glaucoma Relieved by Cocaine Applied to Meckel's Ganglion. Amer. J. Ophth., Dec. '08.

[4]Ransom, S. W.: The Anatomy of the Nervous System. W. B. Saunders Co., 1923, pp. 54-55.

[5]Howell, W. H.: A Text Book of Physiology.

[6]Evans, Sir C. A. L.: Address of the President, Section I, Physiology. Brit. Assn. Adv. Sci., 1928; Science, Sept. 21, '28.

[7]Adson, A. W. and Brown, G. E.: Treatment of Raynaud's Disease by Lumbar Ramisection and Ganglionectomy and Perivascular Sympathetic Neurectomy of Common Iliacs. J. A. M. A., 84: 1908-1910 (June 20) 1925.

[8]Sluder, Greenfield: Nasal Neurology, Headaches and Eye Disorders. C. V. Mosby Co., St. Louis, 1927.

[9]Gundrum, L. K.: Asthma and Eczema Controlled Throught Nasal Ganglion. Ann. Clin. Med., 4:572-573, Jan., '26.

[10]Brandon, W. R.: Contractured Ulnar Paralysis Relieved by Treatment of the Nasal Ganglion. Arch. Otolar, 4:493-494, 1926.

[11]Byrd, H.: Chorea. Arch. Otolar, 7:257-258, (March), 1928.

[12]Crile, G. W.: A Bipolar Theory of Living Processes. The MacMillan Co., 1926.

A Comparison of the Diagnostic Value of the Wassermann, Kahn and Micro-Precipitation Tests for Syphilis*

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THE diagnosis of syphilis by serological methods has become universal. Indeed, the tendency on the part of clinicians is to rely solely, or almost so, on the findings of the serologist. In hospital practice it is becoming common to have a serological test performed routinely on all patients. In our experience this is excellent practice, and a good axiom for adoption would be "a reliable serological test for syphilis should be performed on every new patient." In a large percentage of instances the clinical discovery of a previous syphilitic infection is well-nigh impossible, and a thoroughly reliable test will uncover many such cases. We do not advocate that the results of the test be used as the sole criterion of treatment, but the test or tests may be used as a reliable diagnostic procedure. In any event the results of the test should stimulate the clinician to search for corroborative findings by physical examination and through the medium of a carefully taken history. In view of the difficulties obstructing the clinical detection of syphilis, and also in view of the large number of patients being treated for conditions in which a careful inquiry for a syphilitic infection is not made, as, for example, in accidents, surgical conditions and a variety of infections, a test which will disclose the presence of a syphilitic infection is of prime importance. Whether or not the syphilis so discovered bears any relation to the complaints of the patient is, of course, a matter for the attending physician to decide. Since the adoption of routine Wassermann and precipitation tests in this hospital there have been discovered many latent and old cases of syphilis, the presence of which was entirely unsuspected by the physician. The value of such discoveries has, of course, been of inestimable value to surgeons and physicians alike, and we feel has aided in clearing up many puzzling and obscure clinical syndromes and complications.

Such tests must have a very high degree of accuracy. The discovery of syphilis will increase as the sensitivity of the tests increase. With this in mind we performed Wassermann, Kahn and two micro-precipitation tests.

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One of the latter called for Kahn's antigen and is conveniently labelled in this paper the Micro Kahn test; the other is the micro-precipitation test of Kline, called here the Kline test. The use of the term Micro Kahn is solely for convenience and does not imply any relationship to the standard Kahn test. The only thing common to both tests is the use of the same antigen. These tests were performed on several groups of sera and the results of the tests compared with each other and with the clinical data obtained from the attending physician in all of those cases giving a positive reaction in any one test and in any degree.

In the first four series the Wassermann technique called for two antigens. One of these was a cholesterinized alcoholic extract of dried beef heart made in the laboratory, and the other was Kolmer's cholesterinized lecithinized alcoholic extract of heart muscle, and was obtained from Dr. Kolmer's laboratory. In the fifth series a third antigen was added, namely, the antigen obtained from Dr. Kline, the same as was used in his micro-precipitation test. We found Kline's antigen thoroughly reliable and satisfactory. The Wassermann technique included a primary incubation of complement and antigen in an ice-water bath at 6° to 8° C. Final readings were made after incubation of the system in a water-bath at 37° for 15 minutes. Fresh sheep cells and fresh pooled guinea pig complement were obtained each day for most of the tests. Complement and amboceptor were titrated daily. Antigen controls were set up with each group of sera, as well as known 4 plus and negative sera. Amboceptor was standardized against a 1:10 dilution of complement and 0.5 c.c. of 5% sheep cells. The greatest dilution of amboceptor which gave complete hemolysis after 15 minutes incubation in a water-bath at 37° C. was used as the standard. All sera were inactivated for 20 minutes at 56° C. for the Wassermann and precipitation tests.

For the Kahn test we used the antigen supplied by the Michigan State Board of Health and followed the technique laid down by Dr. Kahn.[1] Readings were made after 15 minutes' incubation in a water-bath at 37° C. The micro-precipitation test with Kahn's antigen was performed according to the technique described by Kline and Young,[2] and read after 10 minutes' incubation at 37° C. Kline's micro-precipitation test was performed according to the technique described by Kline and Young,[3] and employed the very sensitive emulsion of an antigen obtained from Dr. Kline. These were not incubated, but were read after 3 minutes rotation of the slides.

There are three points of view from which the results of these studies may be compared. They may be compared from the standpoint of relative agreement with each other, of absolute agreement with each other, and, thirdly, their agreement with the clinical findings and hence their relative sensitivity.

Accepting a difference of negative to 1 plus or more and 1 plus to 3 plus or more as disagreements gives an index of comparative value and demonstrates the percentage of relative agreement. Such an analysis cannot be considered indicative of the true

sensitivity of the tests, but may be considered as an index of practical value to the clinician, and as reasonably accurate. Thus, in Table I, Part A, 319 specimens were examined by a two-antigen Wassermann and the Kahn tests. The percentage of agreement was 99.06%. In Part B of the same table is given the result of the same Wassermann test with the Kahn and Micro Kahn tests performed on 635 specimens. There was a total agreement of 96.7% and a disagreement of 0.629% between the Wassermann and Kahn; 3.46% between the Wassermann and Micro Kahn, and the same difference between the Kahn and Micro Kahn. The differences occasioned by the introduction of the micro-precipitation test are of significance and will be discussed later. In Part C are the results of the Wassermann, Kline and Kahn tests performed on 1,244 specimens. A total agreement of 96.78% was obtained. In this series the percentage of disagreement between the Wassermann and Kahn tests was 1.45%; between the Wassermann and Kline tests 2.01%; and between the Kahn and Kline tests 2.41%.

In Table II the results of these tests performed on 4,473 specimens are given. This series includes the three groups given in Table I, with in addition two groups comparing the two micro-precipitation tests with the Wassermann and one group in which the three-antigen Wassermann was employed. In this second table the disagreements are based on a difference of 1 plus in any test. Thus, a 3 plus Wassermann and a 4 plus Kahn is considered a disagreement. Hence, the figures given below record the absolute differences and are a true index of the sensitivity of the various tests. Therefore, the percentage of agreement is lower than in Table I.

Of the 4,473 specimens, 462 gave a positive reaction in at least one of the

TABLE I.

DIFFERENCES OF 0-1 PLUS OR MORE, & OF 1 PLUS-3 PLUS OR MORE CONSIDERED DISAGREEMENTS. COMPARISON BETWEEN WASSERMANN'S AND KAHN'S

	COMPARISON BETWEEN WASSERMANN'S AND KAHN'S		
A.	Total Number. 319	Percentage of Agreement. 99.06	
	COMPARISON BETWEEN WASSERMANN'S, KAHN'S, AND MICRO KAHN'S		
B.	Total Number. 635	Percentage of Agreement. 96.7	Percentage of Disagreement Wass. & Kahn ..... 0.629 Wass. & Micro Kahn ..... 3.46 Kahn & Micro Kahn 3.46
	COMPARISON BETWEEN WASSERMANN'S, KLINE'S AND KAHN'S		
C.	Total Number 1,244	Percentage of Agreement. 96.78	Percentage of Disagreement Wass. & Kahn ..... 1.45 Wass. & Kline ..... 2.01 Kahn & Kline 2.41

tests, and as low as a 1 plus is considered a positive reaction for the purpose of this analysis. 141 of these latter were positive in the same degree in all of the tests performed, and all were syphilitics, according to information obtained from the attending physicians. 321 specimens showed differences in the degree of reaction, hence a total disagreement of 7.13%.

In the 321 disagreements, 234 were in sera from syphilitic patients, the other 87 were from nonsyphilitics and from those about whom no information could be obtained. The relative sensitivity of the various tests is shown in Table III, which is based on the disagreements recorded in Table II. In our hands, the Wassermann was slightly more sensitive than the Kahn test, the Micro Kahn more sensitive than the Kahn, and the Kline more sensitive than any of the other three tests. Both the Micro Kahn and Kline tests, however, were positive in more nonsyphilitic sera than the Kahn or Wassermann tests. This is better shown in Tables IV and V. Table IV is a record of the disagreements in a group of known syphilitic patients, but includes only those in which a negative reaction was obtained in one test and a positive in the others. Numbers 2, 3, and 43 in this table are rechecks, but are included since a negative reaction and an anticomplementary reaction were obtained on one occasion. In this group the Kline test proved to be most sensitive in 20 of 34 tests; the Micro Kahn in 4 of 10 tests; the Wassermann in 7 of 45 tests; and the Kahn in 2 of 45 tests.

In Table V are recorded the results obtained on a group of sera from nonsyphilitic patients and those about which we had no clinical data. We

TABLE II.

Number of Reactions	4,473	Reactions 4 Plus in All Tests	115
Negative Reactions	4,011	Reactions 3 Plus in All Tests	12
Positive Reactions	462	Reactions 2 Plus in All Tests	5
		Reactions 1 Plus in All Tests	9
Total Disagreement—7.13%		Positive Agreements (All Known Syphilitics)	141

Number of Disagreements (Based on a Difference of 1 Plus in Any Test) 321
(233 of These Are Known Syphilitics)

	Wass. & Macro Kahn.	Wass., Macro Kahn, & Micro Kahn	Wass., Macro Kahn, & Kline. (2-Antigen Wass.)	Wass., Micro Kahn, & Kline	Wass. & Kline	Wass., Macro Kahn, & Kline. (3-Antigen Wass.)
Total Reactions ..	319	635	832	592	1,184	911
Neg. Agreements .	284	575	767	517	1,060	808
Pos. Agreements .	15	12	21	9	43	41
Disagreements ...	20 (17*)	48 (37*)	44 (29*)	66 (43*)	81 (58*)	62 (50*)

*—syphilitic

must assume, for the purpose of this report, that the positive reactions were false, hence the Kline test gave a falsely positive reaction in 15 of 31 tests, the Wassermann and Kahn in 3 each of 44 tests, and the Micro Kahn in 3 of 12 tests.

These tables indicate that the Kline test is more sensitive in syphilitics, but also gives more falsely positive reactions. However, in view of the experience we have had, as demonstrated in Tables II, III, and IV, we are disposed to believe that many of these patients may be syphilitic. We therefore consider that the results of the test should not be lightly considered and passed over. Indeed, a positive reaction in any test, provided it is performed correctly, is sufficient justification for a recheck, and a persistently positive reaction must be investigated for syphilis with great care. A provocative dose of neoarsphenamine will

TABLE III.

RELATIVE SENSIBILITY OF THE VARIOUS TESTS BASED ON DISAGREEMENTS IN TABLE II

Tests	Disagreements: Total	Disagreements: Number Syphilitic	Relative Sensitivity: Total More Sensitive	Relative Sensitivity: Number Syphilitic	Results Obtained: Wass.	Macro Kahn	Micro Kahn	Kline	Total	Number Syphilitic
Wassermann and Macro Kahn	20	17	10	10						
			10	7						
Wassermann			6	5	Neg.	Neg.	Pos.		10	3
Macro Kahn			3	3	Neg.	Pos.	Pos.		1	0
and	48	37			Pos.	Pos.	Neg.		7	6
Micro Kahn			20	13	Pos.	Neg.	Neg.		1	0
Wassermann			7	6	Neg.	Neg.		Pos.	10	0
(2 antigens)					Neg.	Pos.		Pos.	4	3
Macro Kahn	44	29	1	0	Pos.	Pos.		Neg.	1	1
and Kline			20	8	Pos.	Neg.		Neg.	1	0
Wassermann			20	14	Neg.		Neg.	Pos.	7	2
Micro Kahn			0	0	Neg.		Pos.	Pos.	3	2
and	66	43			Pos.		Pos.	Neg.	1	0
Kline			22	12	Pos.		Neg.	Neg.	2	2
Wassermann			30	24	Neg.			Pos.	18	7
and	81	58			Pos.			Neg.	4	0
Kline			51	37						
Wassermann			8	7	Neg.	Neg.		Pos.	16	10
Macro Kahn			0	0	Pos.	Pos.		Neg.	2	2
and	62	50			Neg.	Pos.		Pos.	6	3
Kline (3-antigen Wassermann)			32	22	Pos.	Neg.		Neg.	2	1

frequently bring about a more strongly positive reaction.

In this connection we find ourselves in total agreement with Kolmer,[4] who states, "The Wassermann, Kahn and all other serum reactions in syphilis are biologically nonspecific, they possess an extremely high degree of practical specificity under proper technical conditions. They are subject to numerous technical errors, and these are almost entirely responsible for falsely positive reactions. The serum diagnosis of syphilis is best served by employing two or more procedures as a complement-fixation and a precipitation test of proved merit. The various serum tests for syphilis are not too sensitive, but rather are not sensitive enough."

The opportunities for technical error are greater in the Wassermann test than in the precipitation tests. But the precipitation tests offer certain difficulties calling for care and experience to overcome. The lower degrees of positiveness are often difficult to estimate. In the micro-precipitation tests false readings may be obtained if the slide is not evenly and uniformly rotated. Too much emphasis cannot be

TABLE IV.

KNOWN SYPHILITICS IN WHICH A NEGATIVE REACTION WAS OBTAINED IN 1 OR MORE TESTS.

No.	Wassermann	Kahn	Micro Kahn	Kline
1	0	2 plus		
2	4 & 3	4 & 3	4 & 0	
3	4 & a. c.	4 & 4	4 & 4	
4	4	4	0	
5	4	4	0	
6	4	4	0	
7	0	0	1	
8	0	0	2	
9	2	2	0	
10	neg.	0	1	
11	neg.	0	1	
12	1	2		0
13	0	0		1
14	0	0		1
15	0	3		3
16	3	0		2
17	0	1		1
18	a. c.	1		2
19	0	1		1
20	0	0		2
21	2	0		2
22	2	0		0
23	1	0		2
24	3	0		0
25	0	0		1 plus
26	2	0		3
27	2	1		0
28	1	0		2
29	0	0		2
30	0	0		2
31	0	0		3
32	2	1		0
33	2	2		0
34	0	1		3
35	0	2		3
36	4	2		0
37	0	0		2
38	0	0		3
39	0	2		4
40	0	1		1
41	4	1		3
42	1	0		2
43	4 & 3	4 & 0		4 & 4
44	0	1		3
45	3	0		4

Wassermann	Most Sensitive in 7 (45 Tests).
Kahn	Most Sensitive in 2 (45 Tests).
Micro Kahn	Most Sensitive in 4 (10 Tests).
Kline	Most Sensitive in 20 (34 Tests).

placed on the care with which the emulsion of the antigen must be made in the Kline test. It is perhaps the most common source of error.

The usefulness of the Kline test perhaps has a wider application than the other precipitation tests. The readings seem to us to have been more distinct and clear cut than those obtained when Kahn's antigen was used. Further, it is not necessary to incubate, and thus evaporation is more easily controlled. The test can be performed quickly and is extremely useful as an emergency measure. It is our practice to do a Kline test on every donor at the same time as the compatibility test is being performed. This gives an excellent control over donors for blood transfusion, and is especially reassuring when donors not on an official list and therefore not subject to test at stated intervals, are used. Nevertheless, we feel that there are always chances for technical error. In this laboratory a stand is taken against being hurried by physicians anxious for their reports. If the test or tests are valuable and worthwhile, they are worth doing well. Accuracy is far more important than speed. Yet there are occasions when the micro-precipitation test may be

TABLE V.
CLINICAL DATA UNKNOWN.

No.	Wassermann	Kahn	Micro Kahn	Kline	No.	Wassermann	Kahn	Micro Kahn	Kline
1	0	1			23	1	0		1
2	0	1			24	0	2		3
3	1	1	0		25	1 or 0	2		2
4	0	0	1		26	2	0		2
5	0 & 0	0 & 0	0 & 2		27	2	0		2
6	0	0	2		28	2			0
7	0	0	1		29	1 or 0	0		1
8	0	0	2		30	1 or 0	0		1
9	0	3			31	1 or 0	0		1
10	0	0	1		32	1 or 0	0		2
11	0 & 1 or 0 & 0		0 & 1		33	0	0		1
12	1	1	0		34	0	0		1
13	0	0	1		35	0	1 or 0		2
14	0	0		1	36	0 or 1	0 & 0		0 & 1 or 0
15	0	0		1	37	0	0		1
16	1 or 0	0		1	38	0	0		2
17	0	1		0	39	0	1		2 & 3
18	0	0		1	40	0	0		2
19	0	0		2	41	0	0		3
20	0	0		1	42	0	0		1
21	0	0		2	43	0	0		2
22	0	1		2	44	0	0		2

Considering 2 Plus or Better as Positive:—

Wassermann	Positive in	3 (44 tests)
Kahn	Positive in	3 (44 tests)
Micro Kahn	Positive in	3 (12 tests)
Kline	Positive in	15 (31 tests)

called for. A positive result is enough to warrant considering the individual a syphilitic until further studies can be made. The combined use of the Wassermann and a precipitation test seems to be the best method of serum diagnosis for syphilis. The Kline micro-precipitation test is easier to perform than the Kahn test, and in our hands has proved more satisfactory.

REFERENCES

[1]KAHN, R. L., Serum Diagnosis of Syphilis by Precipitation, Williams and Wilkins, 1925.

[2]KLINE, B. S., and YOUNG, A.M., A Microscopic Slide Precipitation Test for Syphilis, Jour. of the Amer. Med. Assoc., 86:928, 1926.

[3]KLINE, B. S., and YOUNG, A. M., A Microscopic Slide Precipitation Test for Syphilis, Jour. of Lab. & Clin. Med., 12:477, 1927.

[4]KOLMER, J. A., Serum Diagnosis of Syphilis, Jour. of the Amer. Med. Assoc., 93: 1420, 1929.

A Probable Case of Pituitary Disease Among Men of the Old Stone Age

By Harry Gauss, M.D., Denver, Colo.

MAN'S infirmities are as old as man himself; and in some instances the infirmity existed as a potential pathologic state before man's advent on this earth, awaiting his arrival to fasten itself upon him. Man being but a stage of a constantly changing cycle of biologic organisms is heir to the complexities of the struggle for existence that dominates the world. Tuberculosis for example is thought to have existed long before man made his appearance; and arriving man proving susceptible to this already existing disease became afflicted with it. Tuberculosis as a disease antedates man. Human tuberculosis is a subsequent chapter to bovine tuberculosis which follows avian tuberculosis which had its antecedents in the evolutionary history of the disease.

Elsewhere we have expressed the opinion that tuberculosis as a disease "did not arise with civilized man but rather it existed even in the most primitive prehistoric man, although without doubt the social complex of civilization may have modified some of the aspects of its pathology, epidemiology and symptomatology" . . . that it became a disease entity when . . . . "a suitable host appeared on earth upon which the tubercle bacillus was capable of adapting itself as a parasite. It is known that tuberculosis occurs spontaneously in mammals such as in man and cattle; in birds of which fifty-five afflicted varieties have been described; in reptiles such as snakes; in amphibians; in fish such as the carp, etc . . . Tuberculosis as a disease probably occurred in the Cambrian Age as a disease of fish. . . . As the bacteria encountered the evolution of the species they successively adapted themselves to the emerging species; but this adaptation was consummated only through long periods of time." When man appeared in the Cenozoic age, tuberculosis was an old disease, it probably had already existed for some thirty million years.

Moodie places the beginning of disease at a much earlier period than this, "Disease," he states, "doubtless began with the inception of antagonism between two forms of life, and this may have occured as early as the Archeozoic, and disease thus may be as old as life itself."

That man's infirmities are as old as man is definitely proven by the oldest records of man which is the skeletal remains of Pithecanthropus erectus, the ape man of Java, whose age has been estimated at a half million years. A glance at the photograph of his skeletal remains will show that old Pithe-

canthropus himself had his troubles. At the upper end of the left femur along the line of the tendinous attachment of the iliopsoas and pectineus muscles is seen a large exostosis. In all probability old man Pithecanthropus became disturbed when his leg began to swell and he lost speed in the chase, and perhaps had difficulty in avoiding his natural enemies. Who knows that but for the tumor of his leg he might have gone the way of his associates and there would have been no evidence of man of this date, since there have been no other skeletal remains of his associates discovered thus far. So maybe after all we are indebted to that tumor for preserving to us indirectly the oldest record of man thus far discovered. Be it as it may, human pathology is as old as homo sapiens.

So if we presume to interpret a bit of evidence as an instance of pituitary disease which occurred in the Aurignacian or Late Stone Age approximately 20,000 years ago, the concept is at least consistent with established principles of science.

The writer's attention was called to a photograph of a figurine in Obermaier's "Fossil Man in Spain" by J. A. Jeancon of the Smithsonian Institution, to whom the writer is indebted for being stimulated into this effort. The following description of the figurine is given by Professor Obermaier: "The Aurignacian region of western central Europe includes, besides France, the northern part of Spain, Belgium and England, where Aurignacian industry has been found in the cave of Paviland, Glamorganshire, on the west coast of Wales. This region extends east of the Rhine through all central Germany, where the Aurignacian is admirably represented in the cave of Wildscheurer, near Steeten on the Lahn, Rhine Province; in the caves of Sirgenstein, near Schelklingen and of Bockstein, near Langenau, in Würtemberg; and in the cave of Ofnet, Bavaria. There are also many Aurignacian stations in the loess of Lower Austria in the valley of the Danube between Melk and Vienna. Mention may be made of the station of Willendorf, excavated by me in 1908, where a section of loess twenty meters thick was found to contain no less than nine archeologic strata, embracing the entire evolution of the Aurignacian industry and separating one from another by sterile strata. The fauna included the woolly mammoth (frequent), woolly rhinoceros, cave lion, lynx, wolf, fox, Arctic fox, bear, wolverine, hare, wild boar, bison, ibex, chamois, Saiga antelope (?), reindeer stag, giant deer, and horse. The upper stratum, belonging to the Late Aurignacian, contained a figurine eleven centimeters in height, made of porous limestone, well preserved and with traces of pink color. It represents a nude woman with largely developed breasts and hips but no true steatopygy. The hair is arranged in concentric circles around the head; the face, on the other hand, is quite ignored. The legs and arms are very meager being of secondary interest to the artist. The only ornament represented is a sort of bracelet indicated by course dots on the forearm.

With the authenticity of the figurine vouched for by Hugo Obermaier, Professor of Prehistoric Archaeology at

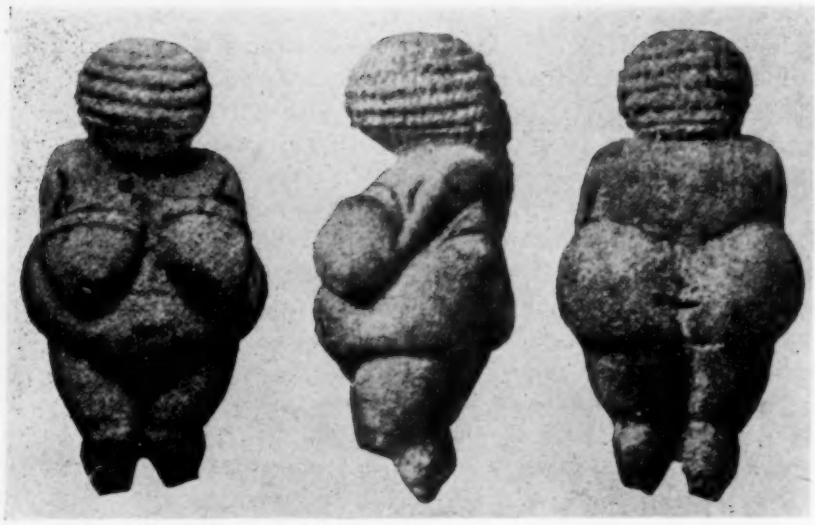


FIG. 1

Figurine of an Aurignacian woman, about 20,000 years old, discovered by Professor Obermaier at Willendorf, Lower Austria, in 1908. The distribution of the excess fat in the subject is suggestive of pituitary disease. Reproduced by permission from Obermaier's "Fossil Man in Spain," courtesy of The Hispanic Society of America.

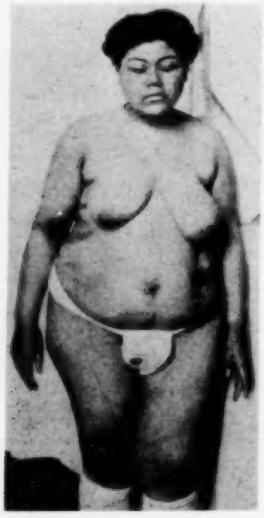


FIG. 2

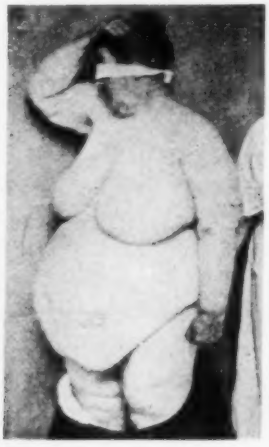


FIG. 3

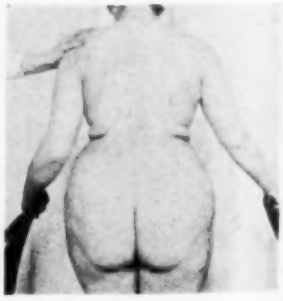


FIG. 4

Some modern prototypes of the Aurignacian woman. Three cases of authenticated pituitary disease taken from Harvey Cushing's "The Pituitary Body," J. B. Lippincott Company, 1912. Reproduced by permission. The photograph on the left is Dr. Cushing's Case No. XXXV, Hypopituitarism of young adult life (dystrophia adiposo-genitalis). The middle photograph is his case No. XXXVII, Adult Hypopituitarism with extreme corpulence and high carbohydrate metabolism. The photograph on the right is his case No. XXXVI, Adult Advancing Hypopituitarism.

the University of Madrid, there remains only its interpretation. Professor Obermaier begins it by stating that it does not conform to any true type of steatopygy probably meaning that it conforms to no known type of racial fatness. Pathologically however the case seems probably of interpretation.

As we look at the figurine we see that it represents a middle aged woman of an extreme obese type. The adipose tissue is distributed in the breasts, abdomen and hips and mons veneris. The neck is short and stocky. The shoulders, arms and legs are not obese.

It becomes evident that this is a case of pathologic obesity. Pathologic obesity is divided into two general groups, exogenous and endogenous. Exogenous obesity is the acquired form which results from excessive food and insufficient exercise; endogenous obesity is the result of a disturbance of one or more of the endocrine glands. Endogenous endocrine obesity is further subdivided into hypothyroidism, hypopituitarism, hypogonadism, pluriglandular and cerebral types. Each of these types has its characteristics which leads to its differential diagnosis. A complete discussion of these characteristics is beyond the scope of this paper. For our purpose it is sufficient to describe the characteristics of the case that concerns us. Falta states under his discussion of Hypophyseal Dystrophy that "the accumulation of fat is chiefly localized to the hips, the buttocks, the mons veneris and the mammae." This description of the localization of excess fat conforms to the localization of the excess fat in the figurine of the Aurignacian woman which dates back about 20,000 years. However in the absence of clinical data it is not possible to make an exact diagnosis. Whether this is a pure case of pituitary disease or whether it is a case of pluriglandular disease cannot be determined, but in all probability the pituitary is involved.

The interpretation of disease from characteristics conveyed in figurines, statues, paintings and other descriptive material has nothing of the unusual in it. There exists a large medical literature dealing with this subject.

In attempting to analyze the Aurignacian figurine we assume, of course, that the artist was faithful in reproducing the characteristics of his subject. Paleolithic man of this period was a skilled artist. Some of his polychrome paintings of animals are excellent likenesses of the subjects portrayed. With reference to the Aurignacian Man, Pirsson and Schuchert state:

"Armed with better weapons of the chase and a wider knowledge of their use, the Aurignacians were able to take better advantage of their environment. Under these circumstances, they had more ease and time for reflection and we witness in them the birth of the fine arts. Sculpture and drawing appear almost simultaneously, and later comes painting. This art we find well preserved in the caves of France and Spain, the art of one period being overlaid by that of later times, and as time goes on the workmanship is greatly improved. Animals of many kinds are depicted, at first outlined in black, then engraved on the walls and even on the ceilings of the dark caves, later were

added polychromes in red, brown, black and several shades of yellow. The pigments were of varied mineral origin and were mixed with grease. These artists also engraved animals on stone, bone and ivory. The human figure appears only in the later paintings, and in these garmented women are seen herding cattle and men chasing wild animals. Small figurines made of ivory and limestone and usually representing nude women, are of still greater antiquity."

For purposes of comparison with existing prototypes, we are reproducing the photograph of the figurine and some authenticated cases of pituitary disease taken from Cushing's "The Pituitary Body." A study of these photographs will show the striking resemblance of the anatomical distribution of the excess adipose tissue in both the figurine and in the modern prototypes. The writer is indebted to The Hispanic Society of America for permission to reproduce the photograph of the figurine and to J. B. Lippincott Company for permission to reproduce the photographs of Dr. Cushing's cases of pituitary disease.

SUMMARY

A figurine of an Aurignacian woman approximately 20,000 years old was found by Professor Obermaier at Willendorf, Lower Austria, in 1908. The figurine is eleven centimeters in height, made of porous limestone, well preserved and with traces of pink color. It represents a nude woman with largely developed breasts and hips, buttocks and mons veneris. The distribution of the excess adipose tissue indicates the presence of a pathologic obesity which is probably endocrine in origin. It conforms anatomically with the distribution of excess fat encountered in dysfunction of the pituitary gland. It probably represents a case of pituitary dysfunction. Man's infirmities are as old as man.

REFERENCES

CUSHING, HARVEY: The Pituitary Body, J. B. Lippincott Company, Philadelphia, 1912.

FALTA, WILLIAM: Endocrine Disease, P. Blakiston's Son & Co., Philadelphia, 1923.

GAUSS, HARRY: The Chemotherapy of Tuberculosis, Colorado Medicine, 1921, 18, 79.

MOODIE, ROY L.: Paleopathology, University of Illinois Press, Urbana, Illinois, 1923.

OBERMAIER, HUGO: Fossil Man in Spain, Yale University Press, New Haven, 1924.

Editorial

THE ANNUAL CLINICAL MEETING

Next month in Baltimore the College will hold its Fifteenth Annual Clinical Meeting. We are approaching that period when we might be said to be reaching our adolescence. The early struggles of organization are over. The College has shown that it has a definite place in the medical structure of the country: it has survived all opposition and destructive criticism, and now approaches its manhood with confidence and with the optimism and constructive eagerness of youth. It is beginning to feel its strength, and looks about for some satisfying outlet for its growing vigor and energy. Growing pains manifest themselves. What shall be its ultimate function? Has it ahead of it a more sharply defined position in the medical life of the country than it now possesses? It has now a highly perfected organization which is working smoothly and successfully; it increases its size each year at a normal and healthful rate; it conducts a yearly meeting, the last several sessions of which have distinguished themselves as offering the best and most stimulating programs of any medical association in the country; its plan of local clinics in the various medical centers in which these annual convocations are held offers a unique opportunity to its Fellows and Associates for an intimate contact with the clinical leaders of the country; it publishes a Journal, the usefulness and influence of which extend far beyond the confines of the College and its members; and it has recently stimulated medical research in internal medicine by the establishment of the John Phillips Memorial Prize. When we have counted these achievements off on our fingers we have told the story of the College and its work up to the present time. Only in one, but that a very important way, has the College had any spiritual influence upon Internal Medicine in America. The mere fact of the College, a selection of physicians for superior worth and attainments, has a very definite influence in the forming of medical ideals throughout the country, in creating a professional standard. This influence, though impalpable and immeasurable, is none the less a very real power in determining the social position of the internists of the country, and social position is a very potent factor in the determination of life principles and aims. But this influence of the College is wholly intrinsic, invested in it primordially by virtue of its very existence, and not the result of a conscious and self-directed effort at influencing the trend of medical thought among the Fellows and Associates, and through them, among the members of the profession as a whole. It seems to the writer

that this constitutes the chief problem of the College at the present time. Iis the College to be satisfied with what it has already accomplished? Is it to go forward year after year, content with its splendid body of representative internists, its successful annual meetings and its journal, and leave no other imprint upon the evolution of medical practice in this country? The writer is sure that the same thought has come to other members of the College in the last year. After all, it has been very fortunate that the energies of the College have been so far expended in perfecting and safe-guarding its organization, and in building a firm foundation for whatever superstructure it may later see fit to add. Fortunately, in these years of development, the College has been singularly free of that type of medical politics which is the reproach of the majority of American medical organizations. The one political aim animating its officers and members has been, up to the present moment, concerned wholly with the establishment of the College on a perfectly sound and safe basis. No ulterior or selfish aims have so far disclosed themselves. Now that the existence of the College has been fully assured, it may be well to consider its future program. What possibilities lie ahead? Into a consideration of these the College should engage itself with great caution and consideration. We have been saved from mistakes by our slowness in developing the functions of the College. We should be in a position to profit through the mistakes made by the American College of Surgeons; and surely we can have no desire to duplicate or parallel that association, either as to ideals or functions. This is not said in a critical way, but stated simply as a fact. We should be able to accomplish something far more noteworthy and significant for the development of internal medicine than that organization has accomplished for surgery, partly because, coming later, we can more fully evaluate the present-day complexities of the situation in which medicine finds itself. Even in the last few years this situation has been clarified in certain of its aspects through much public discussion of questions primarily medical in character. It is true that we have had Committees on Hospitals, Medical Education, Post-graduate Instruction, etc., but nothing has been accomplished by them, and even some of these committees have passed out of existence. This again may be explained by the fact that all our energies were being expended for purposes of self-preservation. We were certainly not prepared to take up constructive work along any one of these lines. Moreover, is it along any one of these that we wish now to go? Is not machinery already furnished by the American Medical Association, the associations of medical colleges, hospitals, etc., to make adequate surveys and studies of such aspects of these problems, as far as internal medicine is concerned? It does not seem that we would be doing anything more than duplication were we to embark upon a special investigation along any one of these lines. All of the questions of medical education and legislation, and of general medical organization in the country seem to be fully taken care of by these various associations, whose

chief duty it is to attend to these problems. If at any time we do not think that certain aspects referring to internal medicine are receiving due attention at their hands, it is within our privilege to call their attention to the fact, and direct them accordingly. It does not seem probable that the College can make any notable contribution directly to questions of education, hospital administration or medical legislation; but it may do much indirectly, by furnishing a body of opinion favoring or opposing any given principle under discussion. Again I think the College is to be congratulated for having escaped useless duplication of effort and energy along the lines originally planned for it. This brings me back to the original question as to the future program of the College. If we are to take a more active part in guiding medical opinion than our present program indicates, it should be along the line, peculiarly fit and appropriate for this society, of influencing the cultural and spiritual side of the general medical mind. We are living in a period in which the soul of the people as a whole is being strongly stirred in regard to social questions as never before. Indeed our modern State is on trial. Social unrest dominates the entire world. Such questions as the dole, bonuses, relief funds, insurance against illness, age and unemployment, cost of medical care, gratuitous medical service, etc., loom more importantly every day. And hints of State Medicine become increasingly louder and bolder. The experience of many physicians during the present year of depression has been very enlightening. They have been made to realize in no pleasant way that medical service is a luxury in over fifty per cent of cases, and a luxury that can be foregone. Hence the empty offices and hospital wards of the present time. In times of prosperity, the practitioner is apt to be a little arrogant in his assumption that medical service is an absolute necessity, and will continue no matter what happens. A year like the present one teaches him otherwise. All of the present-day social unrest affects medicine more intimately than it does any of the other professions. So if deep-rooted changes occur in society at large, medicine must inevitably be deeply involved. Are such changes to occur without thought or discussion of the principles concerned? Should they come, will the men of medicine be prepared to adapt themselves to the inevitable changes that will take place in the machinery of medical practice? Not without much pain, I believe. Does it not behoove us to be in touch with the thought-currents of our times, so that we may acquire an intelligent understanding of the principles and points of view under discussion! We must ultimately stand on one or the other side, and our choice should be one dictated by reason, and not by prejudice or heredity. This is what I mean, when I say that the College should develop the spiritual side of the medical mind in this country. Herein, I believe, lies its greatest possibiilty for good. But this is an intangible program I am at once reminded. Not at all! It would only mean some care and thought in the preparation of our programs, a more serious consideration of speakers on definitely chosen subjects bearing upon the thought-move-

ments of the day, and an opportunity for the College to freely discuss the points of view presented by these speakers. What is needed is to excite interest among the Fellows in these questions. How barren our programs are as far as they reflect the cultural and philosophical sides of medicine. They are too utilitarian, too didactic—only here and there appears an address that concerns itself with something besides diagnosis, case-histories, and treatment. President Musser's address last year was an exception, but my impression was that too many heard it with unheeding ears. The Annual Meeting of the College offers, however, an opportunity for the exchange of opinion, even more satisfactory than that afforded by its programs, and that is the personal contact of Fellows made possible by this yearly coming together. This is after all the highest function of the College, the bringing together for a week of intimate contact the elect of the medical internists from all over the country. What an opportunity is here offered for the sympathetic clashing of personalities, for the interchange of idea and viewpoint. If these personal contacts could only be guided to the discussion of the important matters of the day, instead of motor-car and golf. Those subjects are, however, very important and have their place in our lives. Only not too much place, to the exclusion of even more important things, should be given them. Here again our utilitarian program conspires to defeat our highest function. The European societies are much wiser than we; nearly half of the time given up to their annual meeting is devoted to social affairs—that is to cultural matters. And from such meetings, where the flow of soul has had an even chance with the flow of reason, one comes away refreshed in body and spirit, mentally alert, and awake to the pulsings of his times.

Baltimore As A Medical Center

LAURENCE H. BAKER, Ph.D., *Baltimore, Md.*

SINCE its very foundation, the city of Baltimore has constituted a community in which physicians have been peculiarly prominent, in which physicians have been outstandingly connected with civic and intellectual advances. It is not surprising, therefore, that Baltimore occupies an enviable place in the history of the development of modern medicine. Its contributions to the three great divisions of medical progress—care of the sick, training of succeeding generations of physicians, investigation into the cause and cure of disease—have been of momentous value and have made themselves felt throughout the world.

A brief sketch of the early progress in medicine that the city has seen may be drawn from John R. Quinan: "Medical Annals of Baltimore." There one may learn that Baltimore physicians in 1769, maintained the only inoculating hospital open in America; in 1799 established the sixth State Medical Association in this country; in 1801 disseminated the doctrine of vaccination over the United States; in 1807 established the country's fifth medical college (University of Maryland); in 1839 founded the first College of Dentistry in the world and published the first entirely original work on Dentistry in America; in 1882 established the fourth medical school in the United States for the education of women. In some two pages of fine, continuous print—pages well worth noting—Quinan presents an impressive array of achievements in education, research, and medical and surgical technique. His "Annals," however, cover only the period from 1608 to 1880. The fifty-one years intervening between 1880 and the present added a host of advances no less brilliant and far-reaching.

To enumerate and discuss all these advances would require unlimited space. To present a brief summary, it is no exaggeration to set down the following statements. Baltimore supplies the major portion of the physicians of the State of Maryland, and a surprisingly high percentage of the physicians of the entire country, including its foreign territories and protectorates. This can be verified by checking the Directory of the American Medical Association. On the faculties of the leading medical schools of the country, on the staff of the Rockefeller Institute for Medical Research, in the Public Health Service—even in many of the older faculties abroad—may be found teachers and investigators who secured all or part of their training in Baltimore institu-

tions. Throughout the profession—in both medicine and surgery—there are in use numerous standard procedures, highly effective means of combating discomfort and disease, direct and reliable principles of diagnosis and therapeutics which have had their origin in Baltimore.

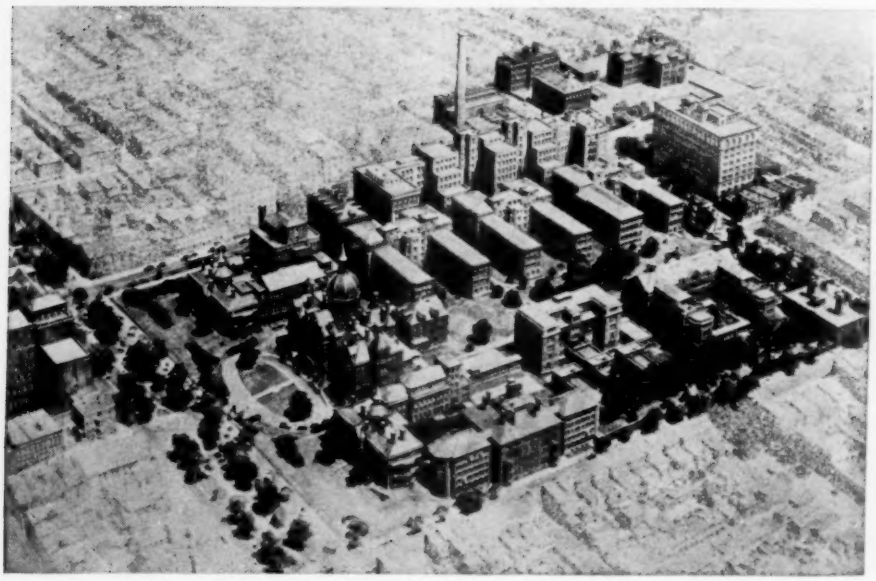
Today the city offers unusual advantages for the student, whether he be aiming at the degree of Doctor of Medicine or seeking further experience and training after attaining that degree. For the sick, who come here from all parts of the world, it offers exceptional facilities for care and treatment. The city contains two of the country's leading schools of medicine. In its inventory of hospitals for Baltimore, the Directory of the American Medical Association lists thirty-five of these institutions.

Of the two medical schools, that of the University of Maryland is the older, dating from 1807. It has behind it a long tradition of successful training of practitioners and investigators; today it is the place whence are graduated most of the physicians who attend the sick of Maryland. This School of Medicine was one of the first to provide for adequate clinical instruction by the erection, in 1823, of its own hospital, The Baltimore Infirmary. Under the name of the University Hospital it still stands on its original site at Lombard and Greene Streets. Its present capacity is 275 beds devoted to general medicine, surgery, obstetrics, and the various medical and surgical specialties. In connection with the hospital, an extensive out-patient department is conducted, two important features of which are the Outdoor Obstetrical Clinic and the Babies' and Children's Clinic. These two perform a valuable service for the public health and social welfare of the community. Modernly equipped clinics have been opened re-

University of Maryland

THE UNIVERSITY HOSPITAL

UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE, SHOWING NEWLY EQUIPPED LABORATORY FOR PATHOLOGY, BACTERIOLOGY, AND CHEMISTRY



JOHNS HOPKINS HOSPITAL GROUP

MEDICAL AND SURGICAL CLINICS, JOHNS HOPKINS HOSPITAL

cently at this Hospital for diseases of the nose and throat and for cancer. This year the Hospital put into service an elaborately constructed air-conditioning apparatus which provides facilities for three patients at once, and admits of careful adjustment of the chemical and physicial properties of the air to suit the individual patient's needs. This apparatus, installed at a cost of $17,500, is a great advantage in cases of respiratory diseases, and in all the many conditions in which is indicated a ready control of atmospheric temperature, humidity and concentration of oxygen and other gases.

The epochal points in the history of both the University of Maryland School for Medicine and the University Hospital were mentioned in these pages last month. Yet there are countless other contacts between these two institutions and medical progress. How many medical men of today think of the University of Maryland when their attention is demanded for tying both carotids at a short interval in the same subject (W. D. MacGill, 1823); ligation of the common iliac artery (W. Gibson, 1812); division of the recti muscles for strabismus (W. Gibson, 1822—seventeen years before Diffenbach); removal of pharyngeal polypus (Tiffany, 1878); excision of the cervix uteri (Jameson, 1823). In the parenthesis are the names of University of Maryland men who performed the operations for the first time, as well as the dates they were performed. It seems not unusual that the first school in this country to introduce an independent chair of diseases of women should be the first in the world to perform a Caesarian Section twice in the same woman, saving mother and child both times. Nor is it surprising that a standard textbook on obstetrics should be written by one of its graduates, J. W. Williams, 1888. In view of the modern popularity of boric acid as an opthalmic antiseptic, it is interesting to note that it received its original application from Samuel Theobald, in 1880, who was a graduate of the University of Maryland. When one think of ovariotomy and kindred operations, it is well to bear in mind that in 1825 the University of Maryland conferred upon Ehpraim McDowell, the father of modern abdominal surgery, his first formal medical degree.

The second medical school, of the city is that of the Johns Hopkins University, dating from 1893. The closest cooperation exists between the Johns Hopkins School of Medicine, The Johns Hopkins Hospital and the Johns Hopkins School of Hygiene and Public Health, so that these three institutions, covering several acres in the eastern section of the city, present one of the world's outstanding centers for medical treatment, teaching and research. Since 1914, the Johns Hopkins School of Medicine has applied the full-time system to its clinical branches; and at the present time all the responsible instructors in Medicine Surgery, Pediatrics, Psychiatry, Ophthalmology and Obstetrics are salaried persons devoting their entire time to university work. From the opening of the school, the preclinical instructors have always been on this basis.

THE WELCH MEDICAL LIBRARY

SARGENT'S PORTRAIT OF THE FOUR DOCTORS: WM. H. WELCH, SIR WILLIAM A. OSLER, HOWARD A. KELLEY, WM. S. HALSTED

The Johns Hopkins Hospital, which has a separate board of trustees and a separate endowment from that of the university, dates from 1889. In construction, it may be termed one of the pavillion types of hospitals, the several major branches of medicine and surgery being housed in separate buildings. Long corridors, however, make the numerous buildings immediately accessible and facilitate the transportation of patients from one point to another without exposure. In growth, the hospital has paralleled quite closely an accretional epic, starting with the dome-topped, red-brick administration building and adding the numerous separate clinics as scientific advances and new funds made them possible. An interesting account of the growth of both the hospital and the school of medicine will be found in the Appendix of the medical school catalogue.

Under the policy of cooperation between hospital and school, the heads of the main clinical services, as well as the director, are members of the medical faculty. The hospital contains 763 beds, and its capacity will be expanded until a total of 950 is reached. The main clinical pavillions are the Marburg Building for Private Patients, the Henry Phipps Psychiatric Clinic, the Harriet Lane Home for Invalid Children, The James Buchanan Brady Urological Institute, the Woman's Clinic, and the Wilmer Ophthalmological Institute. An independent building, completed in 1923, houses the laboratories of pathology and bacteriolgy. The Out-Patient Dispensary and Diagnostic Clinic of the hospital was completed in 1927 at a cost of slightly more than $1,000,000. This dispensary affords, in the lower floors, ample accommodations for a large number of ambulatory patients, with the necessary teaching rooms. On the fifth and sixth floors of the building are housed the laboratory for clinical microscopy and the various other clinical laboratories, including the Kenneth Dows Tuberculosis Research Laboratory. The topmost floors are devoted to the surgical operating rooms.

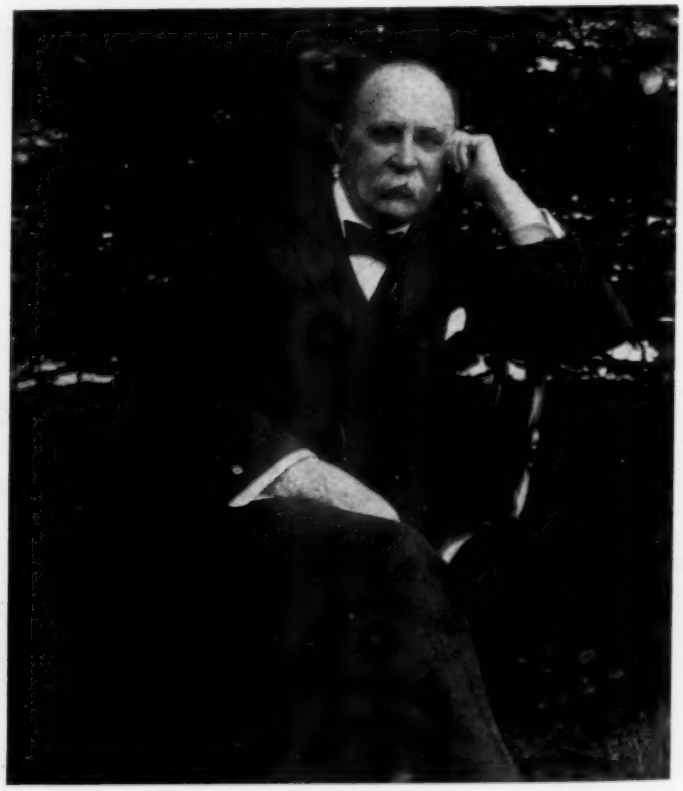
In the autumn of 1929, the William H. Welch Medical Library was opened as the intellectual center of the Hopkings medical group. This library possesses every modern facility for the proper care and collection of medical publications, and houses, on its top floor, an Institute of the History of Medicine.

In course of construction at the present time are two clinics which will modernize and augment the clinical facilities in medicine and surgery. When completed, these will be aptly named the Osler Medical Clinic and the Halsted Surgical Clinic. It is, indeed, difficult to think of Hopkins without thinking of the names of Welch, Kelly, Osler, and Halsted. Even if Sargent's painting of the Four Doctors had never been made, every American physician and surgeon would carry their portraits in his consciousness. Both Hopkins and Baltimore are replete with references to them. A striking illustration of this fact is to be found in the name of the building used as library and executive headquarters by the Medical and Chirurgical Faculty of Maryland —Osler Hall.

A brief description of some of the other hospitals of Baltimore follows:

Baltimore City Hospitals. The Baltimore City Hospitals constitute a group of hospitals founded in 1865, owned by the City of Baltimore, and operated under a single administration. Its component parts are General Hospital, 636 beds; Tuberculosis Hospital, 171 beds; Psychopathic Hospital, 325 beds; Infirmary (Home for the Aged) 854 beds; total 1,986 beds. All beds are free, but if a patient can pay part, he is required to do so. A training school for practical nurses is conducted by the Hospital. This is a pioneer movement, furnishing excellent ministrants for the great number of persons who require trained care but are unable to afford the expenses of a graduate nurse.

Bon Secours Hospital. This is a general hospital, founded in 1919 through the generosity of Mr. and Mrs. George C. Jenkins. Situated away from the conjested centers of the city, it avoids much of the discomfort of noise. The services embrace medicine, surgery, obstetrics, X-Ray, clinical laboratory. There is



Sir William Osler

an out-patient department and a school of nursing. The hospital contains 65 beds and 12 bassinets.

Children's Hospital School. The date of foundation of this institution was 1912. It is maintained by State and City appropriations, private contributions and the receipts from pay patients. The number of beds is 130. In addition to the usual services, it provides for occupational therapy. In the coming year are to be added facilities for heliotherapy and physiotherapy. The age limit for patients is 14 years for either boys or girls. Both white and colored patients are admitted.

Church Home and Infirmary. This hospital occupies the site of the former Washington Medical College. It dates from 1858. Although non-sectarian, the hospital is administered by a board of trustees under the Episcopal Church. Its beds number 176, for treatment of acute cases. In addition to the hospital services there is maintained a home for aged women and also a training school for nurses.

Franklin Square Hospital. Under the name of the National Temperance Hospital of Baltimore, this institution was incorporated in 1898. The present name was adopted in 1901. Its bed capacity is 129. One of its chief aims is to serve patients of moderate means. In conjunction with the hospital a training school for nurses is maintained.

Hospital for the Women of Maryland. This is the only hospital in the State devoted exclusively to the care

West Baltimore General Hospital

South Baltimore General Hospital

Bay View (City Hospitals)

Bon Secour Hospital

Children's Hospital School

Church Home and Infirmary

Franklin Square Hospital

Howard A. Kelly Hospital

Hospital for Women of Maryland (Women's Hospital)

Maryland General Hospital

of sick women. It was incorporated in 1882, and at the present time contains 111 beds and 24 bassinets. Amony its many services are a nurses training school and facilities for post-graduate work in the diseases of women.

Howard A. Kelly Hospital. Established in 1882, this hospital has 35 beds and is engaged principally in radiological and gynecological work. Longer than any hospital in the country it has possessed a substantial supply of radium, its present stock of this precious and potent metal being over five grams. Employing the latest deep therapy X-Ray apparatus and the most modern measuring applicances for both radiological and X-Ray, it is in an unusually favorable position to do all radiological work.

James Laurence Kernan Hospital. In addition to being a hospital, this institution is also an industrial school for children. It contains 62 beds for the active treatment of orthopedic conditions. Recently its facilities have been increased by a new building for operating and physiotherapy of bone and joint cases. Situated on an estate of 75 acres, it has all the advantages of country air and sunshine. A number of the beds are endowed; others are available for private cases, still others are supported by the city and the state.

Mercy Hospital

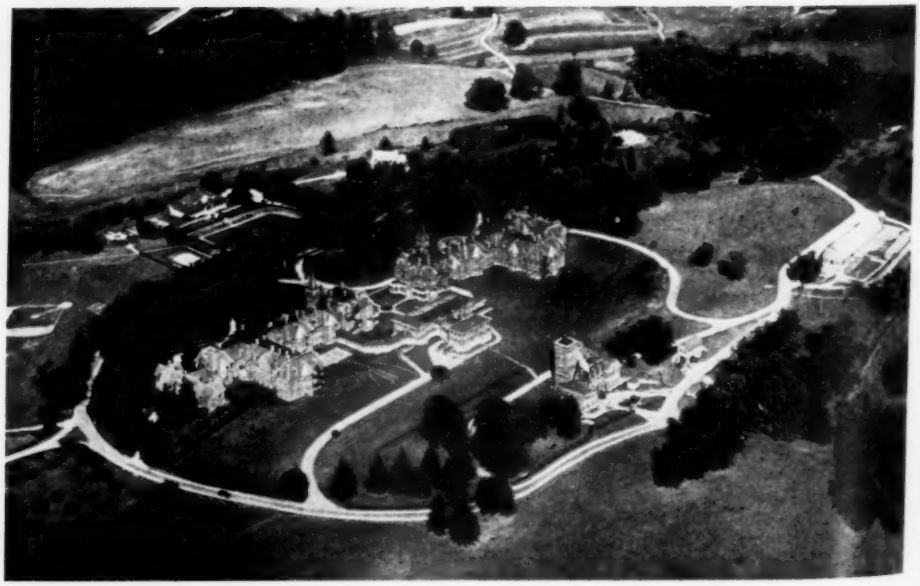
PROVIDENT HOSPITAL

ST. AGNES HOSPITAL

Maryland General Hospital. Owned and operated by the Methodist Hospital Association, Inc., this is a general hospital of 230 beds. Every modern facility is included for surgical and medical measures, and there is a modern department of light therapy. An active out-patient department and a nurses training school are maintained.

Mercy Hospital. Mercy Hospital, as its name implies, is a general hospital conducted by the Sisters of Mercy. It has 90 private rooms and 185 beds available for semi-private and ward patients. Through its affilia-

St. Joseph's Hospital



Sheppard & Enoch Pratt Hospital

tion with the University of Maryland, Mercy Hospital's clinical material, both in its wards and in its out-patient department, is utilized for teaching purposes. Through the generosity of Dr. Waitman F. Zinn, the hospital's facilities have been increased this year by a modern bronchoscopic clinic.

Provident Hospital and Free Dispensary. This hospital contains 125 beds, together with modern operating room, delivery room and X-Ray facilities. It fills a great need in caring for numbers of the sick in Baltimore's fairly large colored population, offering opportunities for internship for graduates of colored schools, and training of colored nurses. In this, it performs a valuable service for the promotion of hygiene among the several states near Maryland in which there is a high percentage of Negroes. Although a goodly number of those admitted are pay patients, much of its work is on a charity basis. The building it occupies is the old site of the Union Memorial Hospital (form-

Sinai Hospital

erly the Union Protestant Infirmary). It has been a colored hospital for the last three or four years.

St. Agnes Hospital. The Sisters of Charity of St. Vincent de Paul conduct this hospital on Mt. Dougherty, Caton and Wilkins Avenues. It is a general hospital with 205 beds and a separate maternity unit. It dates from 1865. Its out-patient department, recently reorganized, does excellent work among the poor of the vicinity.

St. Joseph's Hospital. This hospital, founded by the Sisters of the Third Order of St. Francis, Philadelphia Foundation, dates from 1865. It contains 278 beds and does a large amount of charity work, both in the hospital itself and in the out-patient department.

SYDENHAM HOSPITAL

THE UNION MEMORIAL HOSPITAL. INCORPORATED 1854. REBUILT 1923

U. S. Marine Hospital

The Frederick Bauernschmidt Memorial Building, 1929

Sheppard & Enoch Pratt Hospital. The Sheppard and Enoch Pratt Hospital was founded through the generosity of Moses Sheppard in 1853. In 1903, its endowment was materially increased by Enoch Pratt, a Baltimore philanthropist, hence the two names in its appellation. Today the hospital contains 250 beds and does considerable benevolent work which, in the main, is confined to the residents of Maryland. The work of the hospital is entirely in the field of psychiatry, chiefly in the acute and recoverable illnesses. Habit cases, and cases of undoubted chronicity are not retained. Several members of its staff are included in the faculty of the University of Maryland School of Medicine. It offers facilities for giving specialistic experience, both by physicians and nurses. The site of the hospital is on a tract of 411 acres lying between Charles Street and York Road, some twenty-five minutes by automobile from the center of the city.

The Sinai Hospital. The Sinai Hospital began its existence 63 years ago as the Hebrew Hospital. In 1926 it was entirely renovated. A new pavillion was constructed and the old building was rebuilt for ward work. The cost of the renovation totaled something like a half a million dollars. The number of beds available is 271. The Hebrew Hospital is in the Eastern portion of the city and is a definite element in the great Medical Center developing around Wolfe and Monument Streets. In addition to the usual services it contains departments of Hydrotherapy, Electrocardiography and Occupational Therapy. A feature of its out-patient department in connection with children is the provision for the necessary convalescent care at the Happy Hills Convalescence Home.

Sydenham Hospital. This is the municipal hospital for contagious diseases. Operated under the City Health Department, it is entirely free to local residents. The bed capacity is 110. Much of its clinical material is utilized by the city's two medical schools.

Union Memorial Hospital. Incorporated originally in 1854, this hospital was rebuilt in 1923. The bed capacity is 289. In addition to the usual modern facilities, this hospital contains a wing built and furnished especially for persons of modern means. Both the structure and the endowment of this wing are the gifts of Mr. Frederick Bauernschmit a Baltimore philanthropist.

Were the space available, it would be pleasant to mention the outstanding points in connection with all of Baltimore's many hospitals. To do so, however, would run into considerable length, and even then might omit many valuable salient factors. Suffice it to say that the city offers an abundance of hospital facilities to engage the attention and interests of both the clinician and the laboratory man.

College News Notes

FINAL PROGRAM

FIFTEENTH ANNUAL CLINICAL SESSION—AMERICAN COLLEGE OF PHYSICIANS

GENERAL SESSIONS
Baltimore, Md.—March 23-27, 1931

OPENING GENERAL SESSION
Monday, March 23, 1931, 2:00 O'clock

The Alcazar

1. Addresses of Welcome.
   Joseph S. Ames, President of Johns Hopkins University.
   Raymond A. Pearson, President of the University of Maryland.
   J. M. H. Rowland, President of the Medical and Chirurgical Faculty of Maryland.
   Louis P. Hamburger,* President of the Baltimore City Medical Society.

2. Reply to Addresses of Welcome.
   Sydney R. Miller,* President of the American College of Physicians.

SYMPOSIUM ON GASTRO-INTESTINAL DISEASE

3. The Clinical Significance of So-Called Chronic Appendicitis.
   Julius Friedenwald,* Baltimore, Md.
   Theodore H. Morrison,* Baltimore, Md.

4. The Early Diagnosis of Neoplasms of the Digestive Tract.
   Thomas R. Brown,* Baltimore, Md.

5. Gastric Secretion.
   A study of electrolyte changes of gastric juice during various phases of secretion in connection with simultaneous corresponding changes in the blood and urine. Also a report on some organic constituents heretofore unreported. (Slides and Charts).
   Lay Martin,* Baltimore, Md.

6. Studies on the Mechanism of the Pain of Peptic Ulcer. (Slides).
   Fred M. Smith,* Iowa City, Iowa.

7. Rheumatoid Arthritis. (Slides).
   Russell L. Cecil, New York, N. Y.
   (Guest)

*F. A. C. P.

SECOND GENERAL SESSION
Monday Evening, March 23, 1931, 8:30 P. M.

The Alcazar

Presiding Officer
Maurice C. Pincoffs,* Baltimore, Md.

SYMPOSIUM OF HEART DISEASE

1. Variation in Manifestations on Rheumatic Fever in Relation to Climate. (Slides).
   Warfield T. Longcope,* Baltimore, Md.
2. On Some Phases of Endocarditis. (Charts).
   William S. Thayer,* Baltimore, Md.
3. Chronic Myocardial Insufficiency: Chronic Non-Valvular Cardiac Diseases and its Therapeutic Management. (Slides).
   Henry A. Christian,* Boston, Mass.
4. The Causation of Cardiac Pain.
   Alexander Lambert, New York, N. Y.
   (Guest)
5. The Therapeutic Use of Oxygen in Heart Disease. (Slides).
   Alvan L. Barach, New York, N. Y.
   (Guest)

THIRD GENERAL SESSION
Tuesday, March 24, 1931, 9 A. M.

The Alcazar

Presiding Officer
George Morris Piersol,* Philadelphia, Pa.

1. The Reaction to Nitrites in the Anginal Syndrome and Arterial Hypertension. (Slides).
   Alex. M. Burgess,* Providence, R. I.
2. The Insulin Coefficient, and Improved Method for the Clinical Control of Diabetes Mellitus. (Slides).
   John R. Williams,* Rochester, N. Y.
3. An Evaluation of the Skin Test in Allergy. (Slides).
   Harry L. Alexander, St. Louis, Mo.
   (Guest)
4. The Trend in Cerebral Localization. (Slides).
   Lewellys F. Barker,* Baltimore, Md.
5. Spontaneous Subarachnoid Haemorrhage.
   A Report of Twenty-Nine Cases. (Slides).
   Wardner D. Ayer,* Syracuse, N. Y.

INTERMISSION
PLEASE VISIT THE EXHIBITS!

6. Post-Vaccination Encephalitis. (Slides).
   Charles Armstrong, Surgeon, U.S.P.H.S., Washington, D. C.
   (Guest)
7. The Many-Sided Question of Protein in Nephritis. (Slides).
   William S. McCann,* Rochester, N. Y.

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*F. A. C. P.

8. Circulatory Adjustments in Cardiovascular Diseases. (Slides).
   Soma Weiss,* Boston, Mass.
9. The Response of the Cardiovascular System to Respiratory Strain. A Measure of Myocardial Efficiency. (Slides).
   Allan Eustis,* New Orleans, La.

FOURTH GENERAL SESSION
Tuesday Evening, March 24, 1931, 8:30 P. M.
The Alcazar

Presiding Officer
William Gerry Morgan,* Washington, D. C.
President of the American Medical Association

SYMPOSIUM ON PUBLIC HEALTH,
MEDICAL PRACTICE AND MEDICAL ECONOMICS

1. The Influence of the Practitioner of Medicine in Guiding the Public towards Health. (Charts).
   Haven Emerson, New York, N. Y.
   Professor of Public Health Administration, College of Physicians and Surgeons, Columbia University.
   (Guest)
2. The Proper Relations between the Practicing Physicians and Health Officers.
   Felix J. Underwood,* Jackson, Miss.
   President of the Southern Medical Association.
3. The Hospital—Its Relation to the Community and to the Medical Profession.
   Winford H. Smith, Baltimore, Md.
   Director of the Johns Hopkins Hospital.
   (Guest)
4. Speaker to be Announced.

FIFTH GENERAL SESSION
Wednesday, March 25, 1931, 9 A. M.
The Alcazar

Presiding Officer
John H. Musser,* New Orleans, La.

1. Complement Fixation in the Diagnosis of Amoebiasis.
   Charles F. Craig,* Colonel, (M.C.), U. S. Army, Washington, D. C.
2. The Treatment of Recurrent Erysipelas. (Slides).
   Harold L. Amoss, Durham, N. C.
   (Guest)
3. Observations on Pneumococcus Type III Pneumonia. (Slides).
   Francis G. Blake,* New Haven, Conn.
4. Experimental Pathology of the Liver. (Slides).
   Jesse L. Bollman, Rochester, Minn.
   (Guest)
5. Clinical Aspects of Portal Cirrhosis. (Slides).
   Albert M. Snell,* Rochester, Minn.

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*F. A. C. P.

INTERMISSION
PLEASE VISIT THE EXHIBITS!

6. The Morbid Anatomy of the Diaphragm. (Slides).
   Baldwin Lucké, Philadelphia, Pa.
   (Guest)
7. Pneumoconiosis; Clinical and X-Ray Aspects. (Slides).
   H. R. M. Landis,* Philadelphia, Pa.
8. Endo-Bronchial Manifestations of Pulmonary Disease. Observation on Bronchoscopic Diagnosis and Treatment. (Lantern slides and moving picture film).
   Gabriel Tucker, Philadelphia, Pa.
   (Guest)
9. Heliotherapy. (Moving picture).
   Alexius M. Forster, Colorado Springs, Colo.
   (Guest)

Evening, 8:00 O'clock

The Alcazar

CONVOCATION OF THE COLLEGE

The General Profession and such of the general public as may be interested are cordially invited. No special admission tickets are required. Evening dress is recommended.

1. Convocation Ceremony.
2. President's Address,
   Sydney R. Miller, Baltimore, Md.

Reception to New Members

An informal Reception to new members will follow immediately after the Convocation exercises, at the back of the Auditorium. Newly inducted Fellows should sign the Roster and secure their Fellowship Certificates during the interim between the Convocation and the Reception.

SIXTH GENERAL SESSION
Thursday, March 26, 1931, 9 A. M.

The Alcazar

Presiding Officer
Francis M. Pottenger,* Monrovia, Calif.

SYMPOSIUM ON ENDOCRINE DISORDERS

NOTE: Papers will be limited to 15 minutes
No intermission possible on account of
Annual Business Meeting.

1. Pathological Classification of Goiter and its Clinical Significance. (Slides).
   Wm. Carpenter MacCarty,* Rochester, Minn.
2. The Management of Patients with Extreme and Atypical Hyperthyroidism. (Slides).
   Frank H. Lahey, Boston, Mass.
   (Guest)

*F. A. C. P.

3. Clinical Studies of Hyperthyroidism before and after Subtotal Thyroidectomy.
   Henry M. Thomas, Jr.,* Baltimore, Md.
   William F. Rienhoff, Jr., Baltimore, Md.
   (Guest)
4. The Use of Quinidine Sulphate in the Treatment of Cardiac Irregularities Due to Hyperthyroidism.
   John P. Anderson,* Cleveland, Ohio.
5. The Vital Hormone of the Adrenal Cortex. (Slides).
   Frank A. Hartman, Buffalo, N. Y.
   (Guest)
6. The Relation of the Parathyroid Glands to Calcium Metabolism. (Slides).
   David Preswick Barr,* St. Louis, Mo.
7. The Etiology and Treatment of Diabetes Insipidus. (Slides).
   Thomas B. Futcher,* Baltimore, Md.
8. Metabolic Factors of Value in the Treatment of Obesity. (Slides).
   Frank A. Evans,* Pittsburgh, Pa.
9. The Questionable Nature of "Luxuskonsumption." (Slides).
   L. H. Newburgh,* Ann Arbor, Mich.

THE ANNUAL GENERAL BUSINESS MEETING of the College will be held immediately after the last paper. All Masters and Fellows are urged to be present. Official reports from the Executive Secretary and Treasurer will be read; new Officers, Regents and Governors will be elected, and the President-Elect, Dr. S. Marx White, will be inducted into office.

Evening, 7:30 O'clock

Lord Baltimore Hotel

THE ANNUAL BANQUET OF THE COLLEGE
(Procure tickets at the Registration Bureau.)

Dr. Lewellys F. Barker,* Baltimore, will act as Toastmaster.
Dr. Wm. H. Welch, Professor of the History of Medicine at Johns Hopkins University School of Medicine, will deliver the chief address.
Following the Banquet, there will be dancing for those who wish to remain.

FINAL GENERAL SESSION
Friday, March 27, 1931, 9 A. M.

The Alcazar

Presiding Officer
S. Marx White,* Minneapolis, Minn.

1. Tachycardia: Its Etiology, Prognosis and Treatment. (Slides).
   Chas. W. Barrier, Fort Worth, Texas.
   (Guest)
2. Allergic Migraine. Based on the Study of 200 Cases. (Slides).
   Ray M. Balyeat,* Oklahoma City, Okla.
3. Colonic Changes in Chronic Arthritis. (Slides).
   W. Howard Dickson, Toronto, Canada.
   (Guest)

*F. A. C. P.

SYMPOSIUM ON ANEMIA

4. Agranulocytosis: Its Classification, with Cases and Comments Illustrating the Leucopenic Trend from 8,000 Blood Counts in the South. (Charts).
Stewart R. Roberts,* Atlanta, Ga.
Roy R. Kracke, Atlanta, Ga.
(Guest)

INTERMISSION
PLEASE VISIT THE EXHIBITS!

5. Diet as a Factor in the Etiology of Anemia. (Slides).
Richard A. Kern, Philadelphia, Pa.
(Guest)

6. The Anemias Associated with Gastro-Intestinal Disorders: Clinical Considerations and the Value of Iron in their Treatment. (Slides).
Chester S. Keefer, Boston, Mass.
(Guest)

7. Clinical and Experimental Observations on the Treatment of Pernicious Anemia with Ventriculin and with Liver Extract. (Slides).
Cyrus C. Sturgis,* Ann Arbor, Mich.
Raphael Isaacs, Ann Arbor, Mich.
(Guest)

8. The Adequate Treatment of Anemia. (Slides).
George R. Minot,* Boston, Mass.
William B. Castle, Boston, Mass.

BALTIMORE PROGRAM

SPECIAL CLINICS AND DEMONSTRATIONS

Clinics and demonstrations will be held in the afternoons from 2:00 to 5:00 daily, Tuesday to Friday, inclusive.

Tickets will be required for each and every one of the special clinics, ward rounds and demonstrations. The co-operation of everyone in securing their clinic tickets will assist greatly in distributing the attendance according to the capacity of each program. It is self-evident that a ward round arranged for twenty-five will lose its value for all if forty or fifty are present. Ticket registration naturally is the only effective method of keeping the attendance within the capacities indicated.

To all members of the College, registration blanks for the clinics and demonstrations will be distributed with the final program. These registration blanks should be filled out and returned to the Executive Secretary. Upon receipt of your application for clinic reservations by the Executive Secretary, *proper tickets will be selected and held for you at the Registration Bureau at Baltimore.* Reservations by mail cannot be made after March 15, but reservations may be made in person at the Registration Bureau on the evening preceding any clinic day. *Guests will kindly register for clinics at the Registration Bureau upon arrival at Baltimore.*

*F. A. C. P.

Tuesday, March 24, 1931

A

JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE

Physiology Building No. 25
(Washington and Monument Sts.)
Lecture Room—Second Floor
(Capacity—90).

Program from the Department of Anatomy of the School of Medicine and the Department of Embryology of the Carnegie Institution of Washington. (Program repeated on Thursday).

2:00-2:20 Endocrines and Reproduction.
C. G. Hartmann.

2:20-2:40 Development of the Mammalian Egg.
G. L. Streeter.

2:40-3:00 Behavior of Living Cells (Motion Pictures).
W. H. Lewis.

3:00-3:30 Human Growth and Human Evolution.
A. H. Schultz.

3:30-5:00 Visit to the Laboratories of the Department of Anatomy (Building No. 22), and the Carnegie Institution, Department of Embryology (Building No. 23, Second Floor).

B

JOHNS HOPKINS HOSPITAL

Department of Pathology
(No Program on Tuesday)

C

JOHNS HOPKINS HOSPITAL

Department of Medicine
Building No. 15, Medical Amphitheatre, 1st Floor
(Capacity—170)

2:00-2:45 Clinic.
J. C. Meakins, Montreal.

2:45-3:30 Clinic.
W. T. Longcope.

3:30-4:15 Medical-Surgical Conference.
T. R. Brown and Dean Lewis.

D

JOHN HOPKINS HOSPITAL

Department of Medicine
Building No. 11, Osler Clinic
(Capacity—25 to each ward)
*Ward Rounds

*D-I Ward I —2:00-3:00 E. P. Carter.
3:00-4:00 L. V. Hamman.

*D-II Ward II —2:00-3:00 T. B. Futcher.
3:00-4:00 E. C. Andrus.

*D-III Ward III—2:00-3:00 S. R. Miller.
3:00-4:00 W. S. Tillett.

*(Separate tickets for each of these three rounds.)

E

JOHNS HOPKINS HOSPITAL
Department of Medicine
Out-Patient Division
Building No. 14, Third Floor, Room No. 302
(Capacity—90).

2:00-2:20 Bundle Branch Block. Exhibition of Cases.
J. T. King, Jr.
2:20-2:40 Non-bacterial Bronchopneumonia. A case report.
H. M. Thomas, Jr.
2:40-3:00 Maternal Lumbo-sacral Plexus Injury during Childbirth.
Orthello R. Langworthy.
3:00-3:20 The Treatment of Syphilis.
J. E. Moore.
3:20-3:40 Syphilitic Juxta-Articular Nodules.
H. H. Hopkins.
3:40-4:00 Syphilitic Aortitis.
J. C. Reisinger.
4:00-4:20 Bone Syphilis.
E. D. Weinberg.
4:20-4:40 Practical Considerations of the Wassermann Reaction.
Albert Keidel.

F

JOHNS HOPKINS HOSPITAL
Department of Medicine
Division of Laboratories
Building No. 15, First Floor, Room No. 9
(Capacity—60)
(Same program repeated on Thursday)

2:00-2:20 Sulphaemoglobinaemia.
G. A. Harrop.
2:20-2:40 A Liver Function Test with Bilirubin.
G. A. Harrop.
2:40-3:00 Present Day Conceptions of Immunity in Syphilis.
A. M. Chesney.
3:00-3:20 Rôle of Trauma in the Localization of Syphilitic Lesions.
T. B. Turner.
3:20-3:40 Specificity of the Diagnostic Tests for Syphilis.
Harry S. Eagle.
4:00-5:00 Informal Conferences and Demonstrations in Chemical Laboratory of Medical Clinic, 5th Floor, Room No. 516, and in Laboratory of Experimental Syphilis, 6th Floor, Room 601.

G

JOHNS HOPKINS HOSPITAL
Department of Obstetrics
Building No. 12, Woman's Clinic, Ground Floor
(Capacity—72)
(Same program repeated on Thursday)

2:00-2:20 Medical Indications for Sterilization.
J. W. Williams.

2:20-2:40 End Results of Chronic Nephritis Complicated by Pregnancy.
H. J. Stander.
2:40-3:00 Diabetes and Pregnancy.
C. H. Peckham.
3:00-3:20 Blood and Urinary Protein in the Toxemias of Pregnancy.
M. J. Eastman.
3:20-3:40 Heart Disease and Pregnancy.
A. F. Guttmacher.
3:40-4:00 The Pituitary Gland and the Internal Genitalia.
I. Hofbauer.
4:00-5:00 Informal Conferences in the Laboratories of the Department of Obstetrics, 4th and 5th Floors, Woman's Clinic.

H

JOHNS HOPKINS HOSPITAL
Department of Pediatrics
Building No. 18, Harriet Lane Home
(Capacity—100)

2:00-2:45 Tuberculosis During the First Year of Life.
E. A. Park.
2:45-3:00 Active Immunization against Tuberculosis with Dead Tubercle Bacilli.
F. F. Schwentker.
3:00-3:15 Treatment of Lye Poisoning.
T. C. Goodwin.
3:15-3:30 Effect of Insulin on Mineral Metabolism in Infantile Malnutrition.
M. I. Rubin.
3:30-3:45 Prognosis of Nephritis in Children.
H. Guild.
3:45-4-15 Case Presentations.
4:15-5:00 Visits to Wards, Dispensary and Laboratories of Harriet Lane Home.

I

JOHNS HOPKINS HOSPITAL
Department of Psychiatry
Phipps Psychiatric Institute
Building No. 19, 2nd Floor
(No Program on Tuesday)

J

JOHNS HOPKINS HOSPITAL
Department of Surgery
Building No. 14, Seventh Floor, Room 722
(No Program on Tuesday)

K

JOHNS HOPKINS HOSPITAL
Department of Ophthalmology
Wilmer Ophthalmology Institute
Building
(Capacity—110)

2:00-2:15 Syphilitic Ocular Lesions.
Alan C. Woods.
2:15-2:30 Ocular Changes in Disturbances of Lipoid Metabolism.
Jonas Friedenwald.

2:30-2:45 Modern Conception of Retinal Detachment with its Relation to Internal Medicine.
Clyde A. Clapp.
2:45-3:00 Fundus Changes in Leukemia.
Leo J. Goldbach.
3:00-4:00 Inspection of Building.

L JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE
Institute of the History of Medicine
Welch Medical Library
Building No. 24, Third Floor
(Capacity—100)
(Same program repeated on Thursday)

2:00-4:00 The Program will be devoted to the general field of the History of Medicine and the Use of a Medical Library.
4:00-5:00 Visit to the Welch Medical Library.

M JOHNS HOPKINS UNIVERSITY SCHOOL OF HYGIENE
(Wolfe & Monument Sts.)
Building No. 26
(Also Building No. 23 vide infra)

*M-I Department of Chemical Hygiene
Building 26, Lecture Hall, First Floor
(Capacity—300)
2:00-3:00 Resumé of results of modern studies on nutrition in this country and abroad. (First Lecture).
E. V. McCollum.

*M-II Department of Physiology
Building 26, Seventh Floor
(Capacity—50)
3:00-5:00 Hemophilia.
Wm. H. Howell.
Ultra-violet Light in Relation to the "Common Cold".
Janet H. Clark.

*M-III Department of Biology
Building 23, Fourth Floor
(Capacity—50)
3:00-5:00 Exhibit and demonstration in human genetics and the constitutional factor in disease, with photographs, records from charts, and apparatus.
Raymond Pearl and W. T. Howard, Jr.

*M-IV Departments of Protozoology, Helminthology and Entomology
Building 26, Fourth Floor
(Capacity—50)
3:00-5:00 Combined demonstration of animal parasites and their vectors.
R. W. Hegner, W. W. Cort and F. M. Root.

*(Separate tickets required for each division)

N UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
Administration Building
(Lombard and Greene Streets)
Chemical Amphitheatre
(Capacity—250)

2:00-2:45 Clinical Pathological Conference: Syphilitic Cardio-vascular Disease.
Wm. W. Love, Jr. and C. G. Warner.
2:45-3:15 Experimental Focal Infection with Associated Cardiac Pathology.
Noble W. Jones, Portland, Ore.
3:15-4:00 Medical-surgical Conference: Pericarditis.
M. C. Pincoffs and A. M. Shipley.
4:00-4:30 Certain Blood-pressure Phenomena in Coronary Artery Disease.
T. N. Carey.

O UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
University Hospital
(Lombard and Greene Streets)
Surgical Amphitheatre—Fourth Floor
(Capacity—90)

2:00-2:45 Medical Clinic.
O. H. Perry Pepper, Philadelphia.
2:45-3:30 Medical Clinic.
Gordon Wilson.
3:30-4:15 Medical Clinic.
Paul Clough.
4:15-5:00 Demonstration of Air-conditioning Rooms.
C. Gill and S. Helms.

P UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
(Lombard and Greene Streets)
Pre-clinical Departments
(No Program on Tuesday)

Q UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
Church Laboratory Building
(Lombard and Greene Streets)
(No Program on Tuesday)

R UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
Mercy Hospital
College Building
Saratoga and Calvert Streets
Saratoga St. entrance; Amphitheatre, Second Floor
(Capacity—120)

2:00-2:45 Medical Clinic.
John H. Musser, New Orleans.
2:45-3:30 Endocrine Clinic.
Harvey G. Beck.
3:30-4:15 Clinic on Rheumatic Pericarditis.
Edgar B. Friedenwald.

S SINAI HOSPITAL
(Monument and Rutland Streets)
Lecture Room—Seventh Floor
(No Program on Tuesday)

T BALTIMORE CITY HOSPITALS
Bay View
(4940 Eastern Avenue)
(No Program on Tuesday)

U UNION MEMORIAL HOSPITAL
(33rd and Calvert Streets)
Nurses Auditorium
(No Program on Tuesday)

V HOWARD A. KELLY HOSPITAL
1418 Eutaw Place
(Capacity—35)

2:00-3:00 Demonstration of apparatus and general discussion of methods of radiation.
Fred West and Curtis F. Burnam.

3:00-3:45 Radiation in Gynecology from the Viewpoint of the Internist.
Howard A. Kelly.

3:45-4:30 Radiation in Nose and Throat Conditions from the Viewpoint of the Internist.
William Neill and Curtis F. Burnam.

W THE CHILDREN'S HOSPITAL SCHOOL
(Green Spring Avenue and 41st Street)
(Capacity—25)

2:30-3:15 The Production of Sterilized Maggots from the Blue-bottle Fly.
Elizabeth Engle.

3:15-4:00 The Treatment of Chronic Osteomyelitis by Means of Maggots.
Wm. S. Baer.

4:00-4:30 The Treatment of Arthritis Deformans with Special Reference to Still's Disease.
Wm. S. Baer and Elizabeth Engle.

X ST. AGNES HOSPITAL
(Caton Avenue near Wilkens Avenue)
(Capacity—50)

2:30-4:30 Symposium on the early clinical diagnosis of cancer, and other features of the cancer problem.
Joseph C. Bloodgood and Members of the Hospital Staff.

Y THE SHEPPARD AND ENOCH PRATT HOSPITAL
(York Road near Towson)
The Reception Building
(Capacity—150)

2:30-2:45 Introductory Remarks.
Ross McC. Chapman.

2:45-3:15 Notes on Medical Histories of Some Mental Patients.
Lewis B. Bliss.

3:15-4:00 Physical Signs and Symptoms Presenting in the Syndrome of Incipient Schizophrenia.
Harry S. Sullivan.

4:00-4:30 Some Psychological Considerations in the Practice of Medicine.
William V. Silverberg.

Wednesday, March 25, 1931

A

JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE
Physiology Building No. 25
(Washington and Monument Streets)
Lecture Room—Second Floor
(Capacity—90)

Programs from the Departments of Pharmacology, Physiology and Physiological Chemistry, School of Medicine. (Program repeated on Friday).

2:00-2:30 Insulin and Other Hormones.
J. J. Abel.

2:30-3:00 Use of the Method of Comparative Physiology in Studying Renal Function.
E. K. Marshall, Jr.

3:00-3:30 The Interrelationship Between Insulin and the Pituitary Secretions.
E. M. K. Geiling.

3:30-4:00 The Development of Indicators by Means of which the Reducing Ability of Living Cells may be Studied.
W. Mansfield Clark.

4:00-5:00 Visit to Laboratories of Departments of Pharmacology, Physiology and Physiological Chemistry.
Demonstrations by W. Mansfield Clark and Barnett Cohen.

B

JOHNS HOPKINS HOSPITAL
Department of Pathology
Building No. 13, Ground Floor, Conference Room
(Capacity—200)

2:00-3:00 Clinical Pathological Conference.
W. S. Thayer and W. G. MacCallum.

3:00-3:30 Studies in Immunity.
A. R. Rich.

3:30-4:00 Experimental Nephritis.
S. S. Blackman.

C

JOHNS HOPKINS HOSPITAL
Department of Medicine
Building No. 15, Medical Amphitheatre, 1st Floor
(Capacity—170)

2:00-2:45 Clinic.
John H. Musser, New Orleans.

2:45-3:30 Clinic
L. F. Barker.

3:30-4:15 Clinic.
E. P. Carter.

D

JOHNS HOPKINS HOSPITAL
Department of Medicine
Building No. 11, Osler Clinic
(Capacity—25 to each ward)
*Ward Rounds

*D-I Ward I —2:00-3:00 G. A. Harrop.
3:00-4:00 P. W. Clough.
*D-II Ward II —2:00-3:00 W. T. Longcope.
3:00-4:00 L. V. Hamman.
*D-III Ward III—2:00-3:00 L. F. Barker.
3:00-4:00 F. R. Ford.

E

JOHNS HOPKINS HOSPITAL
Department of Medicine
Out-Patient Division
Building No. 14, Third Floor, Room No. 302
(Capacity—90)

2:00-2:20 The Diagnosis of Gastro-Intestinal Diseases.
T. R. Brown.
2:20-2:40 The Effect of Varying Types of Gastric Resection on the Secretory Function.
E. H. Gaither and W. F. Rienhoff, Jr.
2:40-3:00 Oesophagoscopy and Gastroscopy in Diagnosis.
E. B. Freeman.
3:00-3:20 Bacteriology and Parasitology of the Human Intestine. Practical Considerations.
M. Paulson.
3:20-3:40 Laboratory Studies on Acne Vulgaris.
L. W. Ketron.
3:40-4:00 Tuberculosis of the Skin.
L. Ginsberg.
4:00-4:20 Allergic Manifestations of the Ringworm Infections.
J. E. Kemp.
4:20-4:40 Pemphigus.
I. R. Pels.

F

JOHNS HOPKINS HOSPITAL
Department of Medicine
Division of Laboratories
Building No. 15, First Floor, Room No. 9
(Capacity—60)
(Same program repeated on Friday)

2:00-2:20 The Clinical Significance of the Electrocardiogram.
E. P. Carter.
2:20-2:40 Heart Failure in Hyperthyroidism.
E. C. Andrus.
2:40-3:00 Myocardial Changes in Hyperthyroidism.
D. McEachern.
3:00-3:20 Syphilitic Aortitis.
B. M. Baker.

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*(Separate tickets for each of these three rounds.)

3:20-3:40 Skin Reactions in Pneumonia.
W. S. Tillett.
3:40-4:00 Pathogenesis of Acute Nephritis.
W. T. Longcope and N. McLeod
4:00-5:00 Informal Conferences and Demonstrations in the Cardiographic Laboratory, 5th Floor, Room 506, and in the Biological Laboratory, 6th Floor, Rooms 606, 618.

G

JOHNS HOPKINS HOSPITAL
Department of Obstetrics
Building No. 12, Woman's Clinic, Ground Floor
(No Program on Wednesday)

H

JOHNS HOPKINS HOSPITAL
Department of Pediatrics
Building No. 18, Harriet Lane Home
(Capacity—100)

2:00-2:45 Clinic.
J. C. Gittings.
2:45-3:15 The Treatment of Anemias of Infancy with Copper and Iron.
H. W. Josephs.
3:15-3:45 The Modern Treatment of Epilepsy.
E. M. Bridge.
3:45-4:15 Case Presentations.
4:15-5:00 Visits to Wards, Dispensary and Laboratories of Harriet Lane Home.

I

JOHNS HOPKINS HOSPITAL
Department of Psychiatry
Phipps Psychiatric Institute
Building No. 19, 2nd. Floor
(Capacity—100)

2:00-2:20 Principles in Choice and Treatment in House Cases.
A. Meyer.
2:20-2:40 Out-Patient Practice.
E. L. Richards.
2:40-3:00 Experimentally Induced Neuroses in Dogs.
W. H. Gantt.
3:00-3:20 Somatic Disorders of Functional Origin.
S. Katzenelbogen.
3:20-4:00 Psycholepsy.
W. S. Muncie.

J

JOHNS HOPKINS HOSPITAL
Department of Surgery
Building No. 14, Seventh Floor, Room 722
(Capacity—150)

2:00-3:00 Arteriovenous Aneurysms.
Dean Lewis.
3:00-3:30 X-ray Burns and their Treatment.
J. Staige Davis.

3:30-4:00 Several Unusual Cases of Spinal Disease.
R. W. Johnson, Jr.
4:00-4:30 Diagnosis and Treatment of Tic Douleureux and Menière's Disease.
W. Dandy.
4:30-5:00 Intestinal Obstruction.
H. B. Stone.

K JOHNS HOPKINS HOSPITAL
Department of Ophthalmology
Wilmer Ophthalmological Institute.
Building No. 16
(No Program on Wednesday)

L JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE
Institute of the History of Medicine
Welch Medical Library
(Wolfe and Monument Streets)
Building No. 24, Third Floor
(No Program on Wednesday)

M JOHNS HOPKINS UNIVERSITY SCHOOL OF HYGIENE
(Wolfe & Monument Sts.)
Building No. 26
(Also Building No. 23 vide infra)

*M-I Department of Chemical Hygiene
Building 26, Lecture Hall, First Floor
(Capacity—300)
2:00-3:00 Resumé of results of modern studies on nutrition in this country and abroad. (Second Lecture).
E. V. McCollum.

*M-II Department of Biology
Building 23, Fourth Floor
(Capacity—50)
3:00-5:00 Exhibit and demonstration in human genetics and the constitutional factor in disease, with photographs, records from charts, and apparatus.
Raymond Pearl and W. T. Howard, Jr.

*M-III Department of Filtrable Viruses
Building 26, Ninth Floor
(Capacity—25)
3:00-5:00 The formation of inclusion bodies in virus III of rabbits; discussion and demonstration with lantern slides.
Roscoe R. Hyde.

*M-IV Departments of Protozoology, Helminthology and Entomology
Building 26, Fourth Floor
(Capacity—50)
3:00-5:00 Combined demonstration of animal parasites and their vectors.
R. W. Hegner, W. W. Cort and F. M. Root.

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*(Separate tickets required for each division)

N UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
Administration Building
(Lombard and Greene Streets)
Chemical Amphitheatre
(Capacity—250)

2:00-2:45 Clinical Pathological Conference: Fat Embolism.
C. Lockard and R. B. Wright.
2:45-3:30 Clinic on Disturbances of Motility.
I. J. Spear.
3:30-3:50 Anatomical Aspects of Apoplexy.
L. Freedom.
3:50-4:10 Clinical Types of Apoplexy.
A. C. Gillis.
4:10-4:30 Surgical Aspects of Apoplexy.
C. Bagley.

O UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
University Hospital
(Lombard and Greene Streets)
Surgical Amphitheatre—Fourth Floor
(Capacity—90)

2:00-2:45 Medical Clinic: Pulmonary Tuberculosis.
L. J. Moorman, Oklahoma City.
2:45-3:30 Medical Clinic.
M. C. Pincoffs.
3:30-4:15 Medical Clinic.
H. M. Stein.
4:15-5:00 Demonstration of Air-conditioning Rooms.
C. Gill and S. Helms.

P UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
(Lombard and Greene Streets)
Pre-clinical Departments
(Capacity—25)

*P-I Department of Anatomy, Division of Histology, Embryology and Neural Anatomy. Pathology Building, Second Floor.
2:00-5:00 Demonstration of experimental work on the nature of lung alveoli.
C. L. Davis and J. L. Lutz.
Demonstration of original laboratory apparatus.
C. L. Davis and O. G. Harne.

*P-II Department of Anatomy, Division of Gross Anatomy
Administration Building, Museum Laboratory
2:00-5:00 Demonstrations:
(a) Activation of the thyroid by the anterior lobe hormone in animals.
S. S. Schwartzback, E. Uhlenhuth and H. W. Eisenbrandt.
(b) Activation of the human thyroid by the anterior lobe hormone.
A. V. Duckwall, T. B. Aycock and E. Uhlenhuth.

*(Separate tickets required for each division.)

(c) The blood circulation of the endocrines demonstrated by the injection method.
F. M. Figge.
(d) Human dissections demonstrating the anatomic innervation of the veins.
M. A. Teitelbaum and E. Euhlenhuth.

Q UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
Church Laboratory Building
(Lombard and Greene Streets)
(No Program on Wednesday)

R UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
Mercy Hospital
College Building
(Saratoga and Calvert Streets)
Saratoga St. entrance; Amphitheatre, Second Floor
(Capacity—120)

2:00-2:40 Clinical Pathological Conference: Coronary Thrombosis.
C. C. W. Judd and Standinsh McCleary.
2:40-3:10 The Appendicitis Problem.
Alexius McGlannan.
3:10-3:40 Brain Abscess.
Charles Bagley, Jr.
3:40-4:00 Purulent Perimeningitis.
D. J. Pessagno.
4:00-4:15 Discussion of a Case of Sino-auricular Block.
T. C. Wolfe.

S SINAI HOSPITAL
(Monument and Rutland Streets)
Lecture Room—Seventh Floor
(Capacity—75)

2:00-2:40 Medical Clinic.
James S. McLester, Birmingham.
2:40-3:20 Medical Clinic.
Charles R. Austrian.
3:20-3:40 Spontaneous Hemorrhage into the Adrenals of the Newborn—Report of a Case.
John A. Askin.
3:40-4:00 Congenital Abnormalities.
A. J. Schaffer.
4:00-4:20 An Unusual Case of Bichloride of Mercury Poisoning.
Jos. E. Gichner.
4:20-4:40 Narcolepsy—A Case Report.
J. S. Guttmacher.
4:40-5:00 Case of Thallium Poisoning.
M. Sherry.

T

BALTIMORE CITY HOSPITALS
Bay View
(4940 Eastern Avenue)

*T-I Ward A
(Capacity—30)
2:30-4:30 Medical Clinic and Ward Rounds.
Thomas R. Boggs and Staff.

*T-II Tuberculosis Hospital
(Capacity—25)
2:30-4:30 Diagnostic and Therapeutic Ward Rounds.
C. C. Habliston, T. B. Aycock and Staff.

U

UNION MEMORIAL HOSPITAL
(33rd and Calvert Streets)
Nurses Auditorium
(Capacity—200)

2:00-2:45 The Diagnosis of Traumatic and Suppurative Cerebral Diseases from the Standpoint of the Physician.
Wells P. Eagleton.

2:45-3:15 Remarks on Peptic Ulcer.
J. M. T. Finney.

3:15-3:40 Denervation of the Ureter. A Clinical and Anatomical Study. Report of Cases. Lantern Slides.
L. R. Wharton.

3:40-4:00 The Treatment of Angina Agranulocytica.
L. P. Hamburger and C. A. Waters.

4:00-4:20 Avertin Anaesthesia.
J. Arthur York.

4:20-4:40 The Medical Aspects of Choroiditis.
Cecil Bagley.

V

HOWARD A. KELLY HOSPITAL
(1418 Eutaw Place)
(No Program on Wednesday)

W

THE CHILDREN'S HOSPITAL SCHOOL
(Green Spring Avenue and 41st Street)
(No Program on Wednesday)

X

ST. AGNES HOSPITAL
(Caton Avenue near Wilkens Avenue)
(No Program on Wednesday)

Y

THE SHEPPARD AND ENOCH PRATT HOSPITAL
(York Road near Towson)
(The Reception Building)
(No Program on Wednesday)
Thursday, March 26, 1931

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*(Separate Tickets required for each division)

Thursday, March 26, 1931

A JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE
Physiology Building No. 25
(Washington and Monument Streets)
Lecture Room—Second Floor
(Capacity—90)

Program from the Department of Anatomy of the Medical School and the Department of Embryology of the Carnegie Institution of Washington. (Same program as on Tuesday).

2:00-2:20 Endocrines and Reproduction.
C. G. Hartmann.

2:20-2:40 Development of the Mammalian Egg.
G. L. Streeter.

2:40-3:00 Behavior of Living Cells (Motion Pictures).
W. H. Lewis.

3:00-3:30 Human Growth and Human Evolution.
A. H. Schultz.

3:30-5:00 Visit to the Laboratories of the Department of Anatomy (Building No. 22), and the Carnegie Institution, Department of Embryology (Building No. 23, Second Floor).

B JOHNS HOPKINS HOSPITAL
Department of Pathology
Building No. 13, Ground Floor, Conference Room
(No Program on Thursday)

C JOHNS HOPKINS HOSPITAL
Department of Medicine
Building No. 15, Medical Amphitheatre, 1st Floor
(Capacity—170)

2:00-2:45 Clinic
O. H. Perry Pepper, Philadelphia.

2:45-3:30 Clinic.
L. F. Barker.

3:30-4:15 Medical-surgical Conference.
C. R. Austrian and R. T. Miller.

Thursday, March 26, 1931 (Continued)

D JOHNS HOPKINS HOSPITAL
Department of Medicine
Building No. 11, Osler Clinic
(Capacity—25 to each ward)
*Ward Rounds

*D-I	Ward I	—2:00-3:00	T. R. Boggs.
		3:00-4:00	H. M. Thomas.
*D-II	Ward II	—2:00-3:00	W. T. Longcope.
		3:00-4:00	G. A. Harrop.
*D-III	Ward III	—2:00-3:00	J. T. King, Jr.
		3:00-4:00	T. R. Brown.
	Isolation	—2:00-3:00	P.H.Long.
		3:00-4:00	W. S. Tillett.

*-(Separate tickets for each of these rounds)

E

JOHNS HOPKINS HOSPITAL
Department of Medicine
Out-Patient Division
Building No. 14, Third Floor, Room No. 302
(Capacity—90)

2:00-3:30 Program from Protein Sensitization Clinic.
2:00-2:30 General Considerations.
L. N. Gay.
2:30-3:00 Presentation of Cases.
L. N. Gay, N. B. Herman and T. F. Daniels.
3:00-3:30 Technique in Diagnosis.
L. N. Gay, N. B. Herman and T. F. Daniels.
3:30-5:00 Program from Diabetic Clinic.
3:30-4:00 Management of Ambulatory Diabetes Mellitus.
E. J. Leopold.
4:00-4:30 Changes in Blood Sugar Curves.
M. I. Gichner.
4:30-5:00 Diabetes Mellitus Complicated with Pregnancy.
Albert Weinstein.

F

JOHNS HOPKINS HOSPITAL
Department of Medicine
Division of Laboratories
Building No. 15, First Floor, Room No. 9
(Capacity—60)
(Same program as on Tuesday)

2:00-2:20 Sulphaemoglobinaemia.
G. A. Harrop.
2:20-2:40 A Liver Function Test with Bilirubin.
G. A. Harrop.
2:40-3:00 Present Day Conceptions of Immunity in Syphilis.
A. M. Chesney.
3:00-3:20 Role of Trauma in the Localization of Syphilitic Lesions.
T. B. Turner
3:20-3:40 Specificity of the Diagnostic Tests for Syphilis.
Harry S. Eagle.
4:00-5:00 Informal Conferences and Demonstrations in Chemical Laboratory of Medical Clinic, 5th Floor, Room 516, and in Laboratory of Experimental Syphilis, 6th Floor, Room 601.

G

JOHNS HOPKINS HOSPITAL
Department of Obstetrics
Building No. 12, Woman's Clinic, Ground Floor
(Capacity—72)
(Same program as on Tuesday)

2:00-2:20 Medical Indications for Sterilization.
J. W. Williams.
2:20-2:40 End Results of Chronic Nephritis Complicated by Pregnancy.
H. J. Stander.

2:40-3:00 Diabetes and Pregnancy.
C. H. Peckham.
3:00-3:20 Blood and Urinary Protein in the Toxemias of Pregnancy.
M. J. Eastman.
3:20-3:40 Heart Disease and Pregnancy.
A. F. Guttmacher.
3:40-4:00 The Pituitary Gland and the Internal Genitalia.
I. Hofbauer.
4:00-5:00 Informal Conferences in the Laboratories of the Department of Obstetrics, 4th and 5th Floors, Woman's Clinic.

H

JOHNS HOPKINS HOSPITAL
Department of Pediatrics
Building No. 18, Harriet Lane Home
(Capacity—100)

2:00-2:45 Clinic on Bone Disorders.
E. A. Park.
2:45-3:05 The Cause of Acidosis Associated with Diarrhea.
L. E. Holt, Jr.
3:05-3:25 The Treatment of Anemias of Infancy with Copper and Iron.
H. W. Josephs.
3:25-3:40 An Unusual Case of Bone Dystrophy.
L. Kajdi.
3:40-4:00 Observations on the Factors Influencing the Toxicity of Ergosterol.
D. H. Shelling.
4:00-4:15 Demonstration of Calcification in Vitro.
P. G. Shipley.
4:15-5:00 Visits to Wards, Dispensary and Laboratories of Harriet Lane Home.

I

JOHNS HOPKINS HOSPITAL
Department of Psychiatry
Phipps Psychiatric Institute
Building No. 19, 2nd Floor
(No Program on Thursday)

J

JOHNS HOPKINS HOSPITAL
Department of Surgery
Building No. 14, Seventh Floor, Room 722
(Capacity—150)

2:00-2:30 Clinic on the Diagnosis and Treatment of Hyperthyroidism.
H. M. Thomas and W. F. Rienhoff, Jr.
2:30-3:00 Pre-operative and Post-operative Treatment of Prostatic Obstruction.
H. H. Young.
3:00-3:30 Medical Aspects of Prostatic Obstruction.
E. C. Andrus.
3:30-3:45 Presentation of Cases of Congenital Urinary Obstruction in Childhood.
W. A. Frontz.
3:45-4:00 Intravenous Therapy in the Treatment of Infections of the Genito-Urinary Tract.
J. A. C. Colston.

K JOHNS HOPKINS HOSPITAL
Department of Ophthalmology
Wilmer Ophthalmological Institute
Building No. 16
(Capacity—110)

2:00-2:15 Color Fields as an Aid in the Diagnosis of Intracranial Lesions.
A. L. MacLean.

2:15-2:30 Ocular Findings in Trichinosis.
Cecil Bagley.

2:30-2:45 The Character of Diabetic and Renal Exudates in the Retina.
Benjamin Rones.

2:45-3:00 Clinical Significance of Choroidal Tubercles.
R. T. Paton.

3:00-4:00 Inspection of Building.

L JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE
Institute of the History of Medicine
Welch Medical Library
(Wolfe and Monument Streets)
Building No. 24, Third Floor
(Capacity—100)
(Same program as on Tuesday)

2:00-4:00 The Program will be devoted to the general field of the History of Medicine and the Use of a Medical Library.

4:00-5:00 Visit to the Welch Medical Library.

M JOHNS HOPKINS UNIVERSITY SCHOOL OF HYGIENE
(Wolfe and Monument Sts.)
Building No. 26
(Also Building No. 23 vide infra)

*M-I Department of Chemical Hygiene
Building 26, Lecture Hall, First Floor
(Capacity—300)

2:00-3:00 Resumé of results of modern studies on nutrition in this country and abroad. (Third Lecture).
E. V. McCollum.

*M-II Department of Biostatistics
Building 26, Third Floor
(Capacity—50)

3:00-5:00 Statistics in Medicine (15 minutes), and special topics "The Number of Typhoid-carriers in New York City" and "Measles Epidemics in Baltimore in a 28-year Period."
S. J. Reed.

*M-III Department of Biology
Building 23, Fourth Floor
(Capacity—50)

3:00-5:00 Exhibit and demonstration in human genetics and the constitutional factor in disease, with photographs, records from charts, and apparatus.
Raymond Pearl and W. T. Howard, Jr.

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* (Separate tickets required for each division)

*M-IV Department of Protozoology, Helminthology and Entomology
Building 26, Fourth Floor
(Capacity—50)

3:00-5:00 Combined demonstration of animal parasites and their vectors.
R. W. Hegner, W. W. Cort and F. M. Root.

N UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
Administration Building
(Lombard and Greene Streets)
Chemical Amphitheatre
(Capacity—250)

2:00-2:45 Clinical Pathological Conference: Thyroiditis and Riedel's Struma.
A. M. Shipley and H. R. Spencer.

2:45-3:30 Clinic on Diabetes.
V. Virgil Simpson, Louisville.

3:30-3:50 Some Studies in the Physiology of Bile.
F. A. Ries.

3:50-4:10 Diagnosis in Biliary Tract Disease.
H. M. Stein.

4:10-4:30 Present Status of the Sedimentation Test.
J. G. Huck.

Thursday, March 26, 1931 (Continued)

O UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
University Hospital
(Lombard and Greene Streets)
Surgical Amphitheatre—Fourth Floor
(Capacity—90)

2:00-2:45 Medical Clinic: Diabetes.
John R. Williams, Rochester, N. Y.

2:45-3:30 Medical Clinic: Hypertension.
W. A. Baetjer.

3:30-4:15 Medical Clinic.
C. C. Habliston.

4:15-5:00 Demonstration of Air-conditioning Rooms.
C. Gill and S. Helms.

P UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
(Lombard and Greene Streets)
Pre-clinical Departments
(No Program on Thursday)

Q UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
Church Laboratory Building
(Lombard and Greene Streets)
(No Program on Thursday)

R UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
Mercy Hospital
College Building
(Saratoga and Calvert Streets)
Saratoga St. entrance; Amphitheatre, Second Floor
(Capacity—120)

2:00-2:45 Clinic on Sickle-cell Anemia.
V. P. Sydenstricker, Augusta.
2:45-3:30 Neurological Clinic.
A. C. Gillis.
3:30-4:15 Medical-surgical Conference on Cases of Hemolytic Jaundice.
H. R. Peters and W. D. Wise.

S SINAI HOSPITAL
(Monument and Rutland Streets)
Lecture Room—Seventh Floor
(No Program on Thursday)

T BALTIMORE CITY HOSPITALS
Bay View
(4940 Eastern Avenue)
(No Program on Thursday)

U UNION MEMORIAL HOSPITAL
(33rd and Calvert Streets)
Nurses Auditorium
(No Program on Thursday)

V HOWARD A. KELLY HOSPITAL
(1418 Eutaw Place)
(Capacity—35)

2:00-2:30 Radiation in Urology.
William Neill.
2:30-3:00 Hodgkin's Disease.
Curtis F. Burnam.
3:00-3:45 Radiation in Skin Diseases.
Edmund Kelly.
3:45-4:30 Radiation in Eye Conditions.
William Neill, Jr.

W THE CHILDREN'S HOSPITAL SCHOOL
(Green Spring Avenue and 41st Street)
(No Program on Thursday)

X ST. AGNES HOSPITAL
(Caton Avenue near Wilkens Avenue)
(No Program on Thursday)

Y THE SHEPPARD AND ENOCH PRATT HOSPITAL
(York Road near Towson)
The Reception Building
(Capacity—150)

2:30-3:00 Case Presentations.
Eleanor B. Saunders.
3:00-3:30 Case Presentations.
Harry M. Murdock.
3:30-4:00 Case Presentations.
Niels L. Anthonisen.
4:00-4:30 Case Presentations.
Alexander R. Martin.

Friday, March 27, 1931

A JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE
Physiology Building No. 25
(Washington and Monument Streets)
Lecture Room—Second Floor
(Capacity—90)

Program from the Departments of Pharmacology, Physiology and Physiological Chemistry, School of Medicine. (Same program as on Wednesday).

2:00-2:30 Insulin and Other Hormones.
J. J. Abel.
2:30-3:00 Use of the Method of Comparative Physiology in Studying Renal Function.
E. K. Marshall, Jr.
3:00-3:30 The Interrelationship Between Insulin and the Pituitary Secretions.
E. M. K. Geiling.
3:30-4:00 The Development of Indicators by Means of which the Reducing Ability of Living Cells may be Studied.
W. Mansfield Clark.
4:00-5:00 Visit to Laboratories of Departments of Pharmacology, Physiology and Physiological Chemistry.
Demonstrations by W. Mansfield Clark and Barnett Cohen.

B JOHNS HOPKINS HOSPITAL
Department of Pathology
Building No. 13, Ground Floor, Conference Room
(Capacity—200)

2:00-3:00 Clinical Pathological Conference.
W. S. Thayer and W. G. MacCallum.
3:00-3:30 Studies in Immunity.
A. R. Rich.
3:30-4:00 Experimental Nephritis.
S. S. Blackman.

C

JOHNS HOPKINS HOSPITAL
Department of Medicine
Building No. 15, Medical Amphitheatre, 1st Floor
(Capacity—170)

2:00-2:45 Clinic.
James S. McLester, Birmingham.
2:45-3:30 Clinic.
W. T. Longcope.
3:30-4:15 Clinic.
C. R. Austrian.

D

JOHNS HOPKINS HOSPITAL
Department of Medicine
Building No. 11, Osler Clinic
(Capacity—25 to each ward)
*Ward Rounds

*D-I	Ward I	2:00-3:00	W. S. Thayer.
		3:00-4:00	T. P. Sprunt.
*D-II	Ward II	2:00-3:00	P. W. Clough.
		3:00-4:00	J. T. King, Jr.
*D-III	Ward III	2:00-3:00	E. P. Carter.
		3:00-4:00	E. C. Andrus.

E

JOHNS HOPKINS HOSPITAL
Department of Medicine
Out-Patient Division
Building No. 14, Third Floor, Room No. 302
(Capacity—90)

2:00-2:30 The Treatment of Diseases of the Gastro-Intestinal Tract.
T. R. Brown.
2:30-3:00 Non-Specific Protein Therapy in Diseases of the Digestive Tract.
Lay Martin.
3:00-3:30 Newer Aspects of some Organic Intestinal Disorders.
M. Paulson.
3:30-4:00 Diagnosis and Treatment of Cardiospasm and Cancer of the Oesophagus.
E. B. Freeman and H. E. Wright.
4:00-5:00 X-Ray Conference.
F. H. Baetjer and B. M. Baker.

F

JOHNS HOPKINS HOSPITAL
Department of Medicine
Division of Laboratories
Building No. 15, First Floor, Room No. 9
(Capacity—60)
(Same program as on Wednesday)

2:00-2:20 The Clinical Significance of the Electrocardiogram.
E. P. Carter.
2:20-2:40 Heart Failure in Hyperthyroidism.
E. C. Andrus.

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*(Separate tickets for each of these three rounds)

2:40-3:00 Myocardial Changes in Hyperthyroidism.
D. McEachern.

3:00-3:20 Syphilitic Arthritis.
B. M. Baker.

3:20-3:40 Skin Reactions in Pneumonia.
W. S. Tillett.

3:40-4:00 Pathogenesis of Acute Nephritis.
W. T. Longcope and N. McLeod.

4:00-5:00 Informal Conferences and Demonstrations in the Cardiographic Laboratory, 5th Floor, Room 506, and in the Biological Laboratory, 6th Floor, Rooms 606, 618.

G

JOHNS HOPKINS HOSPITAL

Department of Obstetrics
Building No. 12, Woman's Clinic, Ground Floor
(No Program on Friday)

H

JOHNS HOPKINS HOSPITAL

Department of Pediatrics
Building No. 18, Harriet Lane Home
(No Program on Friday)

I

JOHNS HOPKINS HOSPITAL

Department of Psychiatry
Phipps Psychiatric Institute
Building No. 19, 2nd Floor
(Capacity—100)

2:00-2:20 Experimental Diabetes Insipidus.
C. P. Richter.

2:20-2:40 Bromide Therapy.
O. Diethelm.

2:40-3:00 The Significance of Meningeal Permeability.
S. Katzenelbogen.

3:00-3:20 Suicide Problems.
Ruth E. Fairbank.

3:20-3:40 The Rôle of the Central Nervous System in the Action of the Metabolism Raising Principle of the Thyroid Gland.
H. G. Wolff.

3:40-4:00 A Comparison of the Use of Stramonium and Hyoscine in Postencephalitic Parkinson Syndrome.
L. Hohman.

4:00 Laboratory Demonstration.
C. Bagley.

J

JOHNS HOPKINS HOSPITAL
Department of Surgery
Building No. 14, Seventh Floor, Room 722
(Capacity—150)

2:00-3:00 Peptic Ulcer: Diagnosis and Treatment.
J. M. T. Finney, Sr.

3:00-3:30 Title to be announced later.
S. J. Crowe.

3:30-4:00 Diagnosis and Treatment of Retroperitoneal Abscesses.
G. Bennett.

4:00-4:30 Responsibility of the Internist in the Early Diagnosis of Renal Stasis.
G. L. Hunner.

4:30-5:00 Pathological Lesions in the Pelvic Organs in Five Hundred Cases of Myomata Uteri.
L. R. Wharton.

K

JOHNS HOPKINS HOSPITAL
Department of Ophthalmology
Wilmer Ophthalmological Institute
Building No. 16
(No Program on Friday)

L

JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE
Institute of the History of Medicine
Welch Medical Library
(Wolfe and Monument Streets)
Building No. 24, Third Floor
(No Program on Friday)

M

JOHNS HOPKINS UNIVERSITY SCHOOL OF HYGIENE
(Wolfe and Monument Sts.)
Building No. 26
(Also Building No. 23 vide infra)

*M-I Department of Chemical Hygiene
Building 26, Lecture Hall, First Floor
(Capacity—300)

2:00-3:00 Resumé of results of modern studies on nutrition in this country and abroad. (Fourth Lecture).
E. V. McCollum.

*M-II Building 26, Eight Floor.
(Capacity—50)

3:00-5:00 Demonstration of Animal Colony and of Specific Types of Malnutrition in Animals.
E. V. McCollum.

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*(Separate tickets required for each division)

*M-III Department of Bacteriology
3:00-5:00 Visit to the Laboratory.
W. W. Ford.
Discussion: Control of abortion bacillus infections in dairy cattle.
S. R. Damon.
Building 26, Fifth Floor
(Capacity—25)
Demonstrations:
Cultures of anaerobes on aerobic plates.
Bettylee Hampil.
Bartonella muris and Eperythrozoon coccoides.
C. P. Eliot.
Spirochetes and fusiform bacilli.
Minnie B. Harris.

*M-IV Department of Immunology.
3:00-5:00 Visit to Laboratory.
G. H. Bailey.
Demonstrations:
Cultures of Amoeba histolytica and Amoeba barrata.
Electrophoresis of bacteria in relation to virulence.
R. L. Thompson.
Antigenic properties of pneumococci.
G. H. Bailey.

*M-V Department of Biology
Building 23, Fourth Floor
(Capacity—50)
3:00-5:00 Exhibit and demonstration in human genetics and the constitutional factor in disease, with photographs, records from charts, and apparatus.
Raymond Pearl and W. T. Howard, Jr.

*M-VI Department of Filtrable Viruses
Building 26, Ninth Floor.
(Capacity—25)
3:00-5:00 The formation of inclusion bodies in virus III of rabbits; discussion and demonstration with lantern slides.
Roscoe R. Hyde.

N UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
Administration Building
(Lombard and Greene Streets)

Chemical Amphitheatre
(Capacity—250)

2:00-2:45 Clinical Pathological Conference: Carbon-Monoxide Poisoning.
L. A. M. Krause and L. Freedom.

2:45-3:00 Fatalities in Bronchial Asthma.
H. Bubert.

3:00-3:20 Cases of Hemothorax.
Jos. E. Gichner.

3:20-3:50 Lung Tumors.
C. C. Habliston.

3:50-4:10 Results with Different Types of Phrenicotomy.
T. B. Aycock.

4:10-4:30 Pulmonary Embolism.
C. G. Warner.

O UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
University Hospital
(Lombard and Greene Streets)

Surgical Amphitheatre—Fourth Floor
(Capacity—90)

2:00-2:45 Medical Clinic—Hodgkin's Disease.
E. H. Falconer, San Francisco.

2:45-3:30 Medical Clinic.
Julius Friedenwald.

3:30-4:15 Medical Clinic.
Wm. S. Love, Jr.

4:15-5:00 Demonstration of Air-conditioning Rooms.
C. Gill and S. Helms.

P UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
(Lombard and Greene Streets)

Pre-clinical Departments

*P-I Department of Pharmacology
Gray Laboratory, Second Floor
(Capacity—50)

2:00-5:00 Demonstrations:

(a) Original colorimetric standards for estimating oxidation products (Adrenalin).
Ruth Musser.

(b) The action of soporifics and of digitalis glucosides upon the heart.
W. H. Schultz and W. E. Evans.

(c) The action of sex-hormones and a demonstration of the Ascheim-Zondek pregnancy test.
H. Schroeder and W. E. Schultz.

(d) Enzyme studies and a demonstration of highly purified pepsin.
F. Steigerwaldt.

(e) Pharmacological studies of lithium and some other uric acid eliminants.
H. Schroeder.

*P-II Department of Physiology
Gray Laboratory, First Floor
(Capacity—35)

2:00-5:00 Demonstration: A Study in the irritability of uterine muscle.
O. G. Harne.

*(Separate tickets required for each division)

Q UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
Church Laboratory Building
(Lombard and Greene Streets)
Lecture Room—First Floor
(Capacity—150)

2:00-2:45 Cerebral Hemorrhage in the Newborn, (with motion pictures).
C. L. Joslin and C. Bagley, Jr.
2:45-3:30 Clinic on common acquired deformities of the lower extremities in childhood and their treatment.
R. W. Johnson, Jr.
3:30-4:00 Diabetes in Childhood.
H. M. Stein.
4:00-4:30 Sinus Disease in Childhood.
E. Looper.
4:30-5:00 Tuberculosis in Childhood.
A. H. Finkelstein.

R UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
Mercy Hospital
College Building
(Saratoga and Calvert Streets)
Saratoga St. entrance; Amphitheatre, Second Floor
(Capacity—120)

2:00-2:45 Clinical Pathological Conference: Psittacosis.
M. C. Pincoffs and Standish McCleary.
2:45-3:15 Treatment of Common Poisonings.
H. R. Peters.
3:15-3:35 Chyluria.
George McLean.
3:35-4:00 The Diazo-test in Uremia.
J. S. Eastland and E. G. Schmidt.
4:00-5:00 (Bronchoscopic Clinic; Hospital Building, 5th Floor).
Bronchoscopic Clinic.
W. F. Zinn.

S SINAI HOSPITAL
(Monument and Rutland Streets)
Lecture Room—Seventh Floor)
(Capacity—75)

2:00-2:40 Medical Clinic.
Moses Barron, Minneapolis.
2:40-3:20 Medical Clinic.
S. Wolman.
3:20-3:40 Vaccine Treatment of Multiple Sclerosis.
I. J. Spear and W. H. Davis.
3:40-4:00 Case Report
Edgar Friedenwald.
4:00-4:20 Skin Lesions Associated with Neisserian Infections.
M. S. Rosenthal.

4:20-4:40 An Unusual Case of Tularemia.
M. G. Gichner.
4:40-5:00 The Vestibular Form of Encephalitis Lethargica.
S. Whitehouse.

T

BALTIMORE CITY HOSPITALS
Bay View
(4940 Eastern Avenue)
(No Program on Friday)

U

UNION MEMORIAL HOSPITAL
(33rd and Calvert Streets)
Nurses Auditorium
(Capacity—200)

2:00-2:45 Medical Clinic.
J. C. Meakins, Montreal.
2:45-3:15 Recent Contributions to Ovarian Physiology.
E. H. Richardson.
3:15-3:35 End Results of Surgery for Gastro-duodenal Ulcer.
E. M. Hanrahan, Jr.
3:35-3:55 Chronic Mononucleosis.
T. P. Sprunt.
3:55-4:15 The Thymus Problem.
D. C. Wharton Smith.
4:15-4:30 The Normal Structure and Circulation of the Thyroid Gland.
W. F. Rienhoff, Jr.
4:30-5:00 Nephritis Complicating Pregnancy.
J. McF. Bergland.

V

HOWARD A. KELLY HOSPITAL
(1418 Eutaw Place)
(No Program on Friday)

W

THE CHILDREN'S HOSPITAL SCHOOL
(Green Spring Avenue and 41st Street)
(No Program on Friday)

X

ST. AGNES HOSPITAL
(Caton Avenue near Wilkens Avenue)
(No Program on Friday)

Y

THE SHEPPARD AND ENOCH PRATT HOSPITAL
(York Road near Towson)
The Reception Building
(No Program on Friday)

BALTIMORE PROGRAM OF ENTERTAINMENT FOR VISITING WOMEN

Monday, March 23, 1931

Morning: Registration at The Alcazar.

Afternoon: Registration at The Alcazar.
5:30 o'clock Gallery Talk at Museum of Art by Florence H. Austrian.

Tuesday, March 24, 1931

Afternoon: 2:45 o'clock. Leave The Alcazar in private motors for drive through Roland Park and Guilford, and a tea given by Mrs. Lewellys Barker and Mrs. Sydney Miller at the William H. Welch Medical Library of the Johns Hopkins University Medical School.

Wednesday, March 25, 1931

Morning: 11:00 o'clock. Walters Art Gallery.

Afternoon: 1:00 o'clock. Lunch at the Women's City Club, 15 W. Mt. Vernon Place, as guests of the local Committee on the Entertainment of Visiting Women.
2:30 o'clock. Sightseeing Tour of Old Baltimore in Gray Line Busses.
4:15 o'clock. Tea at residence of Mr. and Mrs. Blanchard Randall, 8 W. Mt. Vernon Place. Hostesses: Mrs. Maurice Pincoffs and Local Committee.

Thursday, March 26, 1931

Afternoon: 1:15 o'clock. Leave The Alcazar in Gray Line Busses for trip to Annapolis, there to visit the U. S. Naval Academy and also historic houses; the latter will be described in an illustrated talk given by Prof. R. T. H. Halsey in Great Hall of McDowell Hall, St. Johns College.

Evening: 7:30 o'clock. The Annual Banquet to which women guests are cordially invited. (See general program for details).

Friday, March 27, 1931

No special program has been arranged. Information regarding sight-seeing trips, shopping tous, or places for luncheon or other entertainment may at all times be obtained at the Information Desk in The Alcazar.

NOMINATIONS FOR ELECTIVE OFFICERS
1931-32

The Nominating Committee herewith transmits the following nominations for elective officers of the American College of Physicians for the year 1931-32:

President Elect:- Francis M. Pottenger, Monrovia, Calif.
1st Vice President:- Aldred Scott Warthin, Ann Arbor, Mich.
2nd Vice President:- Charles G. Jennings, Detroit Mich.
3rd Vice President:- John A. Lichty, Clifton Springs, N. Y.

January 9, 1931

Respectfully Submitted,
Alfred Stengel, *Chairman*
J. H. Means
James S. McLester
E. B. Bradley
E. L. Crispin

THE JOHN PHILLIPS MEMORIAL PRIZE

The Committee on the John Phillips Memorial Prize anonunces that thirty-one theses were received in competition for the 1931 award. These theses were read separately by each of a Committee of five, and, where deemed necessary, were referred to specially selected referees. The final decision of the Committee and referees is that, in accordance with a condition of the original announcement (namely, "The College reserves the right to make no award of the prize if a sufficiently meritorious piece of work has not been received"), no thesis was deemed sufficiently worthy to warrant the bestowal of the prize this year.

The theses are being returned to the authors with the above announcement. A further announcement concerning the award for 1932 will be made within a few weeks.

COMMITTEE ON FINANCE

In accordance with the resolution adopted at the last meeting of the Board of Regents at Louisville, Ky., on November 11, President Sydney R. Miller has appointed the following Committee on Finance for 1931:

Dr. Clement R. Jones, Chairman, Pittsburgh
Dr. James S. McLester, Birmingham
Dr. Charles F. Martin, Montreal
Dr. Francis M. Pottenger, Monrovia
Dr. Charles G. Jennings, Detroit

Among the responsibilities of the Committee on Finance are: examining annual operating statements, security records, proposed budgets; and to carry on such activities as in their judgment will stimulate Life Membership. This Finance Committee is also instructed to formulate a recommendation to the Board of Regents for fixing a term of service for a standing Finance Committee.

COMMITTEE ON COLLEGE INSIGNIA

In accordance further with another resolution adopted at the Louisville meeting of the Board of Regents on November 11, 1930, President Sydney R. Miller appointed the following Committee on College Insignia to examine a comprehensive recommendation recently submitted by one of the Fellows of the College for a simple and dignified Fellowship and Mastership Insignia that may be used in connection with academic dress. This does not look toward the adoption of academic dress for the Convocations of the College, but rather a suitable insignia that members may attach to the sleeves of their academic gowns when attending academic functions:

Dr. Edgar Erskine Hume, Chairman, M. C., U. S. A., Boston
Dr. E. J. G. Beardsley, Philadelphia
Dr. W. Blair Stewart, Atlantic City

Lt. Col. W. Lee Hart (Fellow) of the Medical Corps of the U. S. Army was recently transferred from York, S. C., to the Army War College at Washington, D. C.

Lt. Col. John T. Aydelotte (Fellow) of the Medical Corps of the U. S. Army has been transferred from the Fitzsimons General Hospital, Denver, Colo., to the American Barracks, Tientsin, China, where he will be stationed for two years, with the status of The Surgeon, U. S. Army Troops, Tientsin, China.

Dr. Grayson E. Tarkington (Fellow), Hot Springs, Ark., is the author of a paper entitled, "Dermatitis Exfoliativa," which appeared in the December Issue of the Hospital Bulletin of the Levi Memorial Hospital.

Gifts to the College Library

Acknowledgement is herewith made of the receipt of the following donations of reprints and books to the College Library of publications by members:

Dr. Lawrason Brown (Fellow), Saranac Lake, N. Y.: 1 book: "Intestinal Tuberculosis" (With Homer L. Sampson);
Dr. C. Frank Brown (Fellow), Dallas, Texas: 1 reprint: "Hypothyroidism in Pregnancy;"
Dr. Hyman I. Goldstein (Associate), Camden, N. J.: 1 reprint: "Hereditary Epis-

taxis; With and Without Hereditary (Familial) Multiple Hemorrhagic Telangiectasia (Osler's Disease);"

Dr. Ray W. Kissane (Fellow), Columbus, Ohio: 3 reprints: "Area of the Body Surface and Measurements of the Normal Heart in Children," "Electrocardiographic Electrodes," "Area of the Body Surface and Measurements of the Normal Heart;"

Dr. Sinclair Luton (Fellow), St. Louis, Mo.: 2 reprints: "The Treatment of Chronic Heart Disease," "Comparison of Methods Used for Estimating the Size of the Heart;"

Dr. William D. Reid (Fellow), Boston, Mass.: 1 reprint: "The Heart in Pregnancy."

Dr. Gerald M. Cline (Fellow), Bloomington, Ill., addressed the College Alumni Club of Bloomington, December 19, on "What a Baby Costs."

Dr. Linn J. Boyd (Fellow), New York, and Editor-in-Chief of the Journal of the American Institute of Homeopathy, is the author of an article, "Kotschau's Scientific Basis of Homeopathy—a Simplified Version," which appeared in the December number of the Journal of the American Institute of Homeopathy.

Dr. Curran Pope (Associate), Louisville, was a guest of honor at the meeting of the Cumberland Valley Medical Society, which met at Harlan, Ky., on December 9. Dr. Pope addressed the Society upon the newer methods of treatment for Chronic Infections and Toxemias by the Induction of Therapeutic Fever and especially upon localized thermic elevation of the temperature of the Liver.

Dr. S. Calvin Smith (Fellow), Philadelphia, Vice President of the Philadelphia County Medical Society, broadcast a talk "What can be done for Heart Disease" from WFAN on October 14. This talk was published in the Weekly Roster and Medical Digest on December 6.

Dr. Sidney D. Wilgus (Fellow), Springfield, Ill., addressed the fifteenth annual meeting of the Indiana Society for Mental Hygiene, December 8, on "Organization of Community Facilities for the Prevention, Care and Treatment of Nervous and Mental Diseases."

Dr. Harry Malcome Hedge (Fellow), Chicago, delivered an address on "Treatment of Common Skin Diseases" before the La Porte County Medical Society held at La Porte (Indiana), November 20.

Dr. Robert M. Moore (Fellow), Indianapolis, addressed the Hamilton County (Indiana) Medical Society, November 11, on "Internal Medicine."

Dr. George F. Pfahler (Fellow), Philadelphia, spoke on "Some Practical Points in the Early Diagnosis of Cancer" at the Seminar of the Philadelphia County Medical Society on Friday, December 12. He was introduced by Dr. James M. Anders (Master), Philadelphia.

Dr. Walter C. Alvarez (Fellow), Rochester, Minn., recently delivered an address on "Problems of Gastro-Enterology" before the Washtenaw County Medical Society, Ann Arbor.

Dr. Chester W. Waggoner (Fellow), Toledo, addressed the Wayne County Medical Society (Detroit), December 2, on "Chronic Duodenal Stasis."

The Oklahoma City Clinical Society was addressed, November 5-7, by Dr. Francis M. Pottenger (Fellow), Monrovia, Calif., on "Importance of Visceral Neurology in General Medicine."

The following Fellows of the College were speakers at the three-day graduate course on heart disease arranged by the Heart Committee of the San Francisco County Medical Society, December 9-11:

Dr. William J. Kerr (Fellow), San Francisco—"Use of Quinidine in Treatment of Cardiac Irregularities;"

Dr. Arthur L. Bloomfield (Fellow), San Francisco, together with several other doctors, demonstrated various types of heart disease.

Dr. L. Napoleon Boston (Fellow), Philadelphia, gave a Health Radio Talk, "Goitre," under the auspices of the Philadelphia County Medical Society, December 16.

Dr. Hans Lisser (Fellow), San Francisco, recently delivered an address on Clinical Endocrinology before a meeting of the Sacramento Society for Medical Improvement.

Dr. Mary O'Malley (Fellow), Washington, D. C., celebrated the twenty-fifth anniversary of her service at the St. Elizabeth's Hospital, and was recently entertained by the medical staff of the hospital. Dr. O'Malley has been clinical director of the women's service since 1917.

Dr. Gerald Webb (Fellow), Colorado Springs, addressed the Chicago Tuberculosis Society, January 8, on "Laennec."

Fellows of the American College of Physicians who participated in the Symposium on Gallbladder Disease, as conducted by Northwestern University Medical School, December 17, before the Chicago Medical Society, were Doctors Andrew C. Ivy and Charles A. Elliott, both of Chicago.

Dr. Virgil E. Simpson (Fellow), Louisville, recently addressed the Southwestern Kentucky Medical Association at Mayfield on "Modern Methods of Handling the Diabetic Patient."

Dr. Simpson also addressed the Tri-County Medical Society (Taylor, Green and Adair Counties, Ky.), December 4, on "Mendelian Law in Relation to Medicine."

Dr. George H. Hoxie (Fellow), Kansas City, Mo., recently conducted a symposium on Early Diagnosis of Tuberculosis at a meeting of the Clay County Medical Society at Excelsior Spirngs.

Dr. George Morris Piersol (Fellow), Philadelphia, addressed the Atlantic County (N. J.) Medical Society, November 14, on "Acute Hepatitis."

Dr. George H. Lathrope (Fellow), Newark, N. J., delivered an address on "Chronic Typhlitis as a Cause of Failure in Operations for Chronic Appendicitis," November 11, before the Sussex County Medical Society.

Dr. Louis Hamman (Fellow), Baltimore, addressed the Seventh District Medical Society at Concord (N. C.) on "The Diagnosis of Coronary Occlusion."

The Mecklenburg County Medical Society (N. C.) was addressed, November 18, by Dr. James B. Bullitt (Fellow), Chapel Hill, on "Ruptured Aneurysm of the Circle of Willis."

Dr. James S. McLester (Fellow), Birmingham, Ala., addressed the Hamilton County (Tenn.) Medical Society, November 20, on "Dietary Management of the Nephritic."

At the annual meeting of the Radiological Society of North America, Dr. Isador S. Trostler (Fellow), Chicago, was reelected Secretary.

Dr. J. C. Waddell (Fellow), Beatrice, Nebr., was elected President of the Cage County (Nebr.) Medical Society at its annual meeting held recently.

Dr. Earle E. Farnsworth (Fellow), Grand Island, Nebr., presented a paper on "The Symptoms and Medical Treatment of Ulcer" at a symposium on Peptic Ulcer presented at the meeting of the Hall County (Nebr.) Medical Society at the Grand Island Clinic.

Dr. George W. Covey (Fellow), Lincoln, Nebr., is the author of an article on "Coronary Thrombosis — A Review of Autopsy Findings" in the January Issue of the Nebraska State Medical Journal.

In the December Issue of the Southern Medical Journal, the following Fellows are authors of articles indicated:

Dr. Sydney R. Miller (Fellow), Baltimore, with Dr. Charles A. Waters (Fellow), Baltimore: "Intravenous Cholecystography and Liver Function Determination: Clinical and Roentgenological Value;"

Dr. Lewis J. Moorman (Fellow), Oklahoma City, Okla.: "Simultaneous Bilateral Pneumothorax."

On December 2, 1930, the Radiologists of Brooklyn, New York, formed an organization which is to be known as the Brooklyn Roentgen Ray Society. Dr. Charles Eastmond (Fellow), Brooklyn, was elected Pres-

ident of the above-named Society. The Society will meet regularly on the first Tuesday of each month, from October to April.

Dr. L. F. C. Wendt (Fellow), Detroit, addressed the members of the Woman's Auxiliary of the Wayne County (Detroit) Medical Society, December 9, on "Essential Value of Food in Diet and Dieting."

Dr. Grafton Tyler Brown (Fellow), Washington, D. C., read a paper on "Perennial Hay-Fever," by invitation, before the Eastern Section of the American Laryngological, Rhinological and Otological Society's meeting in Atlantic City, January 5. The discussion was opened by Dr. Maximilian A. Ramirez (Fellow), New York, N. Y., and Dr. George Piness (Associate), Los Angeles, Calif.

The public schools of the cities of East Chicago and Gary, Indiana, have inaugurated Child Guidance Clinics for their problem children, or children with emotional disorders. Problem school citizens will likely become problem social citizens later. The clinics do not undertake the study of the feeble minded or epileptics. Other organic conditions, however, are studied. Child Guidance has raised the good prognosis rate of problem children from 10% to 50%.

Dr. H. S. Hulbert (Fellow), Chicago, goes to Indiana one day a week to conduct these clinics. Educators, pediatricians, sociologists and psychiatrists are invited to attend these clinics, by making arrangements.

Announcement has been received that the Charles Godwin Jennings Hospital, successor to the Detroit Diagnositic Hospital, has been completed at a cost of $800,000, and was opened on November 28. The new hospital is organized as a non-profit corporation governed by a Board of Trustees. It has forty-two private rooms and twelve double rooms.

Dr. Frank Smithies (Master), Chicago, delivered a public address, December 9, at Wauseon, Ohio, on "What the Public Should Expect from the Hospital and Medical Profession." On December 8, 9 and 10, Dr. Smithies presented clinics on medical and surgical aspects of duodenal ulcer and biliary tract disease at the DeEtte Harrison Detwiler Memorial Hospital at Wauseon. The staff of the Detwiler Memorial Hospital is composed of the entire membership of the Fulton County Medical Society.

Dr. George W. McCoy (Fellow), National Institute of Health, Washington, D. C., is Secretary of the United States Committee of the Second International Congress of Comparative Pathology, which will meet in Paris, France, October 14-18, 1931.

Dr. Miles J. Breuer (Fellow), Lincoln, Nebr., has recently been appointed head of the Department of Pathology of the Bryan Memorial Hospital.

Dr. D. P. Scott (Fellow), Lynchburg, Va., addressed the South Piedmont Medical Society at Danville (Va.), November 25, on "Medical Aspects of Diseases of the Ductless Glands."

At the annual meeting of the Richmond (Va.) Academy of Medicine, Dr. J. Morrison Hutcheson (Fellow) was elected President. Dr. Charles M. Caravati (Fellow) was elected a Vice President, and Dr. Stewart R. Roberts (Fellow), Atlanta, delivered a paper on "Thyroid Heart."

Dr. Warren T. Vaughan (Fellow), Richmond, took part in a symposium on Allergy at the meeting of the Postgraduate Medical Society of Southern Virginia, January 13.

Dr. Mason Romaine (Fellow) Petersburg, Va., was elected President of the Petersburg (Va.) Medical Faculty at its recent meeting in December.

Dr. Paul F. Whitaker (Fellow), Kinston, N. C., was elected a Vice President of the Seaboard Medical Association of Virginia and North Carolina at Elizabeth City, N. C., December 2-4, 1930.

Dr. Stewart R. Roberts (Fellow), Professor of Clinical Medicine at Emory University School of Medicine, Atlanta, addressed the senior medical students of the Medical College of Virginia at Richmond, December 10, on Exophthalmic Goiter.

OBITUARY

Oscar Dowling

Dr. Oscar Dowling, one of the original members of the American College of Physicians and a former president of the Louisiana State Board of Health, was dramatically killed aboard one of the railroad ferries crossing the Mississippi River at New Orleans on the night of January 2, 1931. From the information that the coroner was able to elicit and from deductive reasoning, there being no witnesses of the event, Dr. Dowling evidently while attempting to board the train on the ferry slipped and was carried under the wheels. It was some hours before his body was discovered.

The death of Dr. Dowling removes from the state of Louisiana and the South one of the most active medical men in this section. He was for many years head of the State Board of Health and did a tremendous service in improving sanitation in Louisiana and New Orleans. Dr. Dowling was a fearless prosecutor of what he considered wrong. At times his methods were spectacular, but he went ahead without fear or favor in doing what he thought was right for the community as a whole. He fought persistently and steadily for the elevation of preventive medicine and for public health ideals. Contemporaries who followed Dr. Dowling through his years of service with the State Board of Health testify as to how he improved health conditions in Louisiana and to the difference that exists now as contrasted with conditions when he first took office.

For some years Dr. Dowling was Professor of Hygiene at Tulane University. He served as a member of the Board of Trustees of the American Medical Association for twelve years and was chairman of the Section on Preventive and Industrial Medicine and Public Health in 1924-25. Dr. Dowling had a wide circle of friends throughout the country. These men knew him as a charming, congenial southern gentlemen, one who invariably had definite ideas concerning very broad fields which he never hesitated to advance if he had the opportunity.

(Furnished by J. H. Musser, M.D., New Orleans, La.)

Dr. Edward Franklin Leonard (Fellow), Chicago, Ill., died, October 31, 1930, of heart disease; aged, 58 years.

Dr. Leonard was born at Cincinnati, Ohio. His records show that he matriculated in the College of Physicians and Surgeons of Chicago, the College of Medicine of the University of Illinois, October 3, 1892, upon credentials showing that he had obtained the degree of Doctor of Medicine from the Harvey Medical College of Chicago, Illinois, in June, 1902. Upon these credentials, he was advanced to the fourth year class, and received his degree of Doctor of Medicine from the University of Illinois on May 26, 1903. He was Instructor in Neurology on the Faculty of the College of Medicine of the University of Illinois from 1913 to 1916, when he was advanced to the rank of Assistant Professor,

and remained on the Faculty in this Department until 1921.

Dr. Leonard was the author of many articles published in various medical journals. He was a member of the Chicago Medical Society, the Illinois State Medical Society, the American Medical Association, the Illinois State Hospital Medical Society, the Chicago Neurological Society, and had been a Fellow of the American College of Physicians since January 30, 1920.

Doctor George Morris Golden

The sudden and untimely death from heart disease of Dr. G. Morris Golden on January 12, 1931, marks a distinct loss not only to the Hahnemann Medical College and Hospital of Philadelphia where he was Professor and head of the Department of Medicine but also to the entire medical profession of which he was a distinguished member.

Dr. Golden was comparatively a young man at the height of a successful career. His personality, executive ability and broad scientific knowledge gained for him a reputation among his colleagues and profound admiration by all with whom he came into contact. He was especially loved and respected by his students and patients for whom he gave his all. He was a tireless worker and student himself and invariably believed that the best time to do a thing was now. He disliked procrastination and, for success's sake, Self was a secondary consideration. He was a conscientious observer and thoroughly recorded scientific data, and, although he did not write books, he spoke frequently on medical subjects and contributed extensively and commendably to medical literature through medical journals.

Dr. Golden was born in Philadelphia, Pa., March 14, 1876, educated in the Public Schools and Central Manual Training School and at the University of Pennsylvania. He received his degree in Medicine from the Hahnemann Medical College of Philadelphia in 1899.

Since graduation, he has been associated with the Medical Department of the Hahnemann Medical College and Hospital. For many years he was Clinical Professor of Medicine and for the past five years has been Professor and Head of the Department of Medicine. He was also Chief of the Medical Staff of the St. Luke's and Children's Homeopathic Hospital of Philadelphia and Consulting Physician to several institutions. He was a past President of the Eastern Homeopathic Medical Association and the Homeopathic Medical Society of the State of Pennsylvania.

Dr. Golden was elected to Fellowship in the American College of Physicians in 1929 and was an active member of the Philadelphia County Homeopathic Medical Society, the Homeopathic Medical Society of the State of Pennsylvania, the American Institute of Homeopathy and the Germantown Medical Society. He was also a member of the Unanimous Club of New York, the Fortnightly Club and the Phi Alpha Gamma Fraternity. He is survived by his widow, Mrs. Lorana Mattix Vanneman Golden, two daughters and a twin brother, E. Lewis Golden of Reading, Pennsylvania.

(Furnished by Carl V. Vischer, M.D., F.A.C.P., Philadelphia, Pennsylvania.)